



King's Research Portal

DOI:

[10.1176/appi.ajp.2018.17111199](https://doi.org/10.1176/appi.ajp.2018.17111199)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Bromis, K., Calem, M., Reinders, S., Williams, S. C. R., & Kempton, M. J. (2018). Meta-Analysis of 89 Structural MRI Studies in Posttraumatic Stress Disorder and Comparison With Major Depressive Disorder. *The American Journal of Psychiatry*, 175(10), 989-998. <https://doi.org/10.1176/appi.ajp.2018.17111199>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Supplementary Materials for Meta-Analysis of 89 Structural MRI Studies in Posttraumatic Stress Disorder and Comparison With Major Depressive Disorder

Methods

MEDLINE (Pubmed) search term

The following MEDLINE search term was used and was completed on July 4th 2016. MEDLINE was used because it has excellent coverage of MRI studies of clinical populations, particularly from 1990s forward.

((("Stress Disorders, Traumatic"[MeSH] OR "PTSD" OR "post traumatic stress" OR "posttraumatic stress") AND MRI)

The search terms in the parenthesis were to catch all studies either tagged by the commonly used MeSH term "Stress Disorders, Traumatic" or the free text terms mentioned. Using the text MRI in pubmed then automatically maps this to the more broader search term:

"magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields] OR "mri"[All Fields]

By hand searching through previous reviews and meta-analyses we identified a number of studies however they were all duplicated from the MEDLINE search except for 5 studies (see Figure S1). Further details of how studies were reviewed can be found at <http://www.ptsdmri.uk> which includes a list of the 800 studies in the literature search, indicating which studies were included/excluded and the reasons for exclusion.

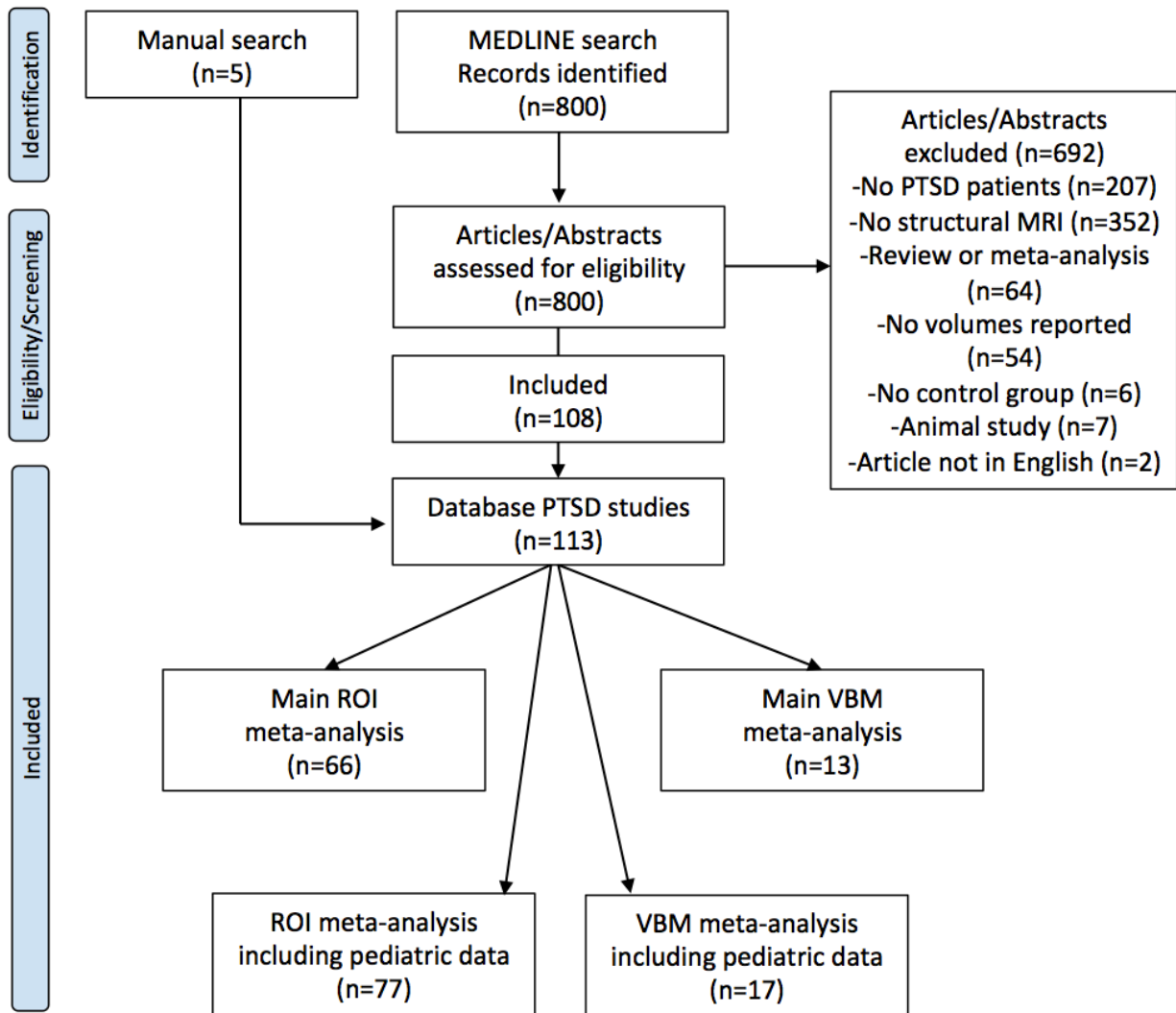


Figure S1: Adapted PRISMA flowchart showing study inclusion. The number of studies included in the meta-analysis including pediatric data is 89 studies (77 region-of-interest studies plus 17 VBM studies, minus 5 overlapping studies)

Database of imaging studies in Post-Traumatic Stress Disorder

Studies were included in the database if patients were diagnosed with PTSD according to standardized diagnostic criteria, and for region-of-interest studies volumetric data was presented in terms of group means and standard deviations, and for VBM studies spatial coordinate data was presented. Control groups differed between studies, the largest proportion used non-traumatised-controls, other studies used a Traumatised-controls and a smaller proportion included two control groups, non-traumatised-

controls and Traumatized-controls. One hundred and thirteen studies satisfied all the criteria and were incorporated in the database (80 region-of-interest studies, 23 VBM studies, and 10 studies presenting both region-of-interest and VBM data).

Data recorded in the database

The following data from each study were included in the database: number of PTSD patients and number of controls, diagnostic classification system used, mean age of patients and controls, number of males and females in the patient and control groups, mean age of illness onset, time since trauma, duration of illness, mean score from Clinician-Administered PTSD Scale (CAPS),¹ and the type of control group used. For medication we recorded the number of patients described as drug free (not necessarily medication naive), using antidepressants, mood stabilizers, or antipsychotics. From the MRI acquisition we recorded slice thickness and magnetic field strength.

Post-traumatic Stress Disorder Region-of-interest Meta-analysis

In order to ensure that the selection of brain structures for the meta-analysis was not biased, we recorded all regions that had been investigated in the 90 studies reporting region-of-interest data included in the database. As observed in previous meta-analyses, exact anatomic definitions of brain structures varied across studies. Where data was unclear or we suspected sample overlap between studies we contacted the authors. Due to the limited information provided by the case-control studies we did not attempt to assess bias in the sample obtainment, although we did analyse publication bias (see below). To ensure that the meta-analysis was sufficiently powered, we included brain regions for which the volume mean and standard deviation in both patient and control groups were reported by three or more studies

Region of interest Sensitivity Analysis

To test how robust the results were to variations in the meta-analysis method, 4 sensitivity analyses were conducted for the region of interest meta-analysis.

(1) For a given region, some authors separately reported left and right measures while others included only the combined total measure. For studies that only reported left and right measurements, we used a previously described method² to calculate the mean and standard deviation for the total volume. The method requires an estimate of the correlation coefficient between the left and right volumes. This coefficient was set to 0.8 but was varied in the sensitivity analysis as 0, 0.5 and 1.0.

(2) While most individual studies reported absolute volumes of brain structures a small number of studies reported volumes divided by intracranial volume. In the main analysis we combined studies reporting absolute volumes, and volumes divided by intracranial volume. In the second sensitivity analysis we excluded volumes divided by intracranial volume

(3) While most individual studies reported volumes of brain structures a small number of cortical regions were reported in terms of thickness. For these regions we combined studies reporting thickness and volume, but excluded thickness measures in the third sensitivity analysis.

(4) In the main analysis we excluded studies with paediatric patients to reduce heterogeneity, in the fourth sensitivity analysis we included 11 paediatric studies.

Combining study estimates

The meta-analysis for each brain structure was performed by using meta-analytical equations entered into Excel (see www.ptsdmri.uk). This technique has the advantage of efficient data entry, being publicly available while using identical equations to the METAN command in STATA,³ which is commonly used in meta-analyses publications. In terms of validation, the method been used in parallel with STATA in three previous meta-analyses^{4,5,6} and produced the same results.

Combining patient subgroups

A minority of studies reported measures from subgroups of patients and their own matched control group. In this case, we considered subgroups as equivalent to separate studies. Similarly, when studies reported men and women in the patient group separately, we incorporated the results in the meta-analysis as two different studies. This method has been used in a previous meta-analysis.⁷ Because the meta-analyses examined a large number of regions and included sub-meta-analyses it is susceptible to type I errors. Therefore, results that survive Bonferroni correction for multiple comparisons are indicated.

Voxel Based Morphometry Meta-analysis using Seed-based d Mapping (SDM)

The following inclusion criteria were applied to the database of 113 studies: 1) gray matter VBM study comparing adult patients with PTSD to either non-traumatised-controls or traumatised-controls; 2) results presented in Talairach or MNI coordinates; 3) studies were only included if a whole brain analysis was performed rather than a small volume correction to ensure no bias in the regions reported. Thirteen

studies met inclusion criteria and are listed in Table S1. We emailed all study authors who used SPM (Statistical Parametric Mapping) to process their data for a 'T-map' image comparing PTSD gray matter volume to the control group. 'T-maps' are three dimensional maps comprising statistical data of volume differences in thousands of voxels in the brain and provide far more detailed information than significant coordinates reported in studies. However, SDM allows both T-maps and coordinates to be combined in a single meta-analysis and the methodology reported in detail by Radua et al.⁸ We received 6 T-maps from 6 independent studies and these were included in the meta-analyses. In addition to the main meta-analysis comparing PTSD to all controls, three additional VBM analyses were conducted: 1) comparing the PTSD group with non-traumatised-controls only 2) comparing the PTSD group with traumatised-controls only, 3) comparing PTSD group with all controls and widening the criteria to include paediatric studies. T-maps and coordinates signifying gray matter volume changes from where we were unable to obtain T-maps were extracted from relevant studies and analysed using Seed-based d Mapping⁸ (SDM version 5.14, <http://www.sdmproject.com>). For studies where coordinate data was used, these were convolved with a Gaussian kernel (FWHM=20mm) in order to optimally compensate the sensitivity and specificity of the analysis. As is standard in SDM analyses, the number of randomizations were set to 100 and a threshold was set at $p < 0.005$ as well as a cluster-level threshold of 10 voxels in order to increase sensitivity and correctly control false-positive rate.⁸ A jackknife sensitivity analysis was performed in order to assess the robustness of the results which was achieved by excluding one study in each of the analyses.

Results

Region of interest sensitivity analysis:

4) Including paediatric data

Eleven pediatric studies were included in the region of interest meta-analysis. In the analysis comparing PTSD patients to all controls there were 11 new significant results: smaller frontal lobe, gray matter, cerebral volume, right and total temporal lobe, right amygdala, cerebellum, vermis, and the anterior midbody, posterior midbody and isthmus of corpus callosum (Table S5, Figure S5a-S5b). The reduction in the volume of the left anterior cingulate was no longer significant. In the PTSD vs non-traumatised-controls comparison, 11 new significant results emerged with the pediatric data: PTSD patients had significant smaller intracranial volume, right and total temporal lobe, total and left amygdala, cerebellum, vermis and anterior midbody, posterior midbody, isthmus and total cross sectional area of the corpus callosum (Table S6, Figure S6). There was no change in significance for the PTSD vs traumatised-controls or traumatised-controls vs non-traumatised-controls comparison.

Table S1. Database of PTSD MRI studies					
Study	No. of PTSD Patients	No. Non-Traumatised Controls (NTC)	No. Traumatised Controls (TC)	Diagnostic Criteria	Mean Patient Age, y
Bremner et al (1995)	26	22	ns	DSM-III-R	46
Gurvits et al (1996)	7	8	7	DSM-III-R	44.4
Bremner et al (1997)	17	17	ns	DSM-III-R	40.1
De Bellis et al (1999)	44	61	ns	DSM-III-R	12.2
Bonne et al (2001)	10	ns	27	DSM-IV	33.7
Carrion et al (2001)	24	24	ns	DSM-IV	11
De Bellis et al (2001)	9	9	ns	DSM-IV	10.6
Schuff et al (2001)	18	19	ns	DSM-IV	51.2
De Bellis et al (2002)	28	66	ns	DSM-IV	11.47
De Bellis et al (2002)	43	61	ns	DSM-IV	12.2
Fennema-Notestine et al (2002)	11	17	11	DSM-IV	33.35
Gilbertson et al (2002)	12	23	23	DSM-IV	ns
Villareal et al (2002)	12	10	ns	DSM-IV	43
Bremner et al (2003)	10	11	12	DSM-IV	35
De Bellis et al (2003)	61	122	ns	DSM-IV	11.74
Hedges et al (2003)	4	4	ns	DSM-IV	54.5
Rauch et al (2003)	9	ns	9	DSM-IV	52
<i>Yamasue et al (2003)</i>	<i>9</i>	<i>ns</i>	<i>16</i>	<i>CAPS</i>	<i>44.6</i>
Lindauer et al (2004)	14	ns	14	DSM-IV	35.4
May et al (2004)	20	24	23	DSM-IV	52.3
Pederson et al (2004)	17	17	17	DSM-IV	24.8
Shin et al (2004)	8	ns	8	DSM-IV	50.5
Villareal et al (2004)	12	10	ns	DSM-IV	43
Wignall et al (2004)	15	11	ns	DSM-IV	43
Winter et al (2004)	15	15	15	DSM-IV	42
Thomas et al (2004)	61	121	ns	DSM-IV	11.74
<i>Corbo et al (2005)</i>	<i>14</i>	<i>14</i>	<i>ns</i>	<i>DSM-IV</i>	<i>33.36</i>
Golier et al (2005)	14	20	13	DSM-IV	70.5
Lindauer et al (2005)	18	ns	14	DSM-IV	39.6

Table S1. Database of all PTSD MRI studies (1/4, continues over 4 pages) ns = not stated/ not recruited. Rows in BOLD indicate studies included in the PTSD region-of-interest meta-analysis, rows in italics indicate studies included in the VBM meta-analysis, rows in both BOLD and italics indicate studies included in both the region-of-interest and VBM meta-analyses, rows in normal typeface were not included in either meta-analysis.

Table S1. Database of PTSD MRI studies (continued)

Study	No. of PTSD Patients	No. Non-Traumatised Controls (NTC)	No. Traumatised Controls (TC)	Diagnostic Criteria	Mean Patient Age, y
<i>Chen et al (2006)</i>	12	ns	12	DSM-IV	34.56
De Bellis et al (2006)	58	98	ns	DSM-IV	12
Emdad et al (2006)	23	17	ns	DSM-IV	38.7
Freeman et al (2006)	10	6	10	DSM-IV	79.6
Jatzko et al (2006)	15	15	ns	DSM-IV	48.2
Kitayama et al (2006)	8	13	ns	DSM-IV	43
Lindauer et al (2006)	12	ns	12	DSM-IV	35.1
Richert et al (2006)	23	24	ns	DSM-IV	11
Tupler et al (2006)	61	122	ns	DSM-IV	11.75
Woodward et al (2006)	51	ns	48	DSM-IV	45.25
Levitt et al (2006)	18	23	22	DSM-IV	52.5
Li et al (2006)	12	ns	12	DSM-IV	34.56
Kitayama et al (2007)	9	9	ns	DSM-IV	37.8
Pavic et al (2007)	15	15	ns	DSM-IV	32
Woodward et al (2007)	51	ns	48	DSM-IV	45.25
Yehuda et al (2007)	17	ns	16	DSM-IV	60.6
Hakamata et al (2007)	14	70	100	DSM-IV	45.6
Bonne et al (2008)	22	22	ns	DSM-IV	36
Bossini et al (2008)	34	34	ns	DSM-IV	38
Geuze et al (2008)	25	ns	25	DSM-IV	35.08
Hara et al (2008)	15	15	15	DSM-IV	44.8
<i>Kasai et al (2008)</i>	18	23	23	DSM-IV	52.8

Table S1 (Continued). Database of PTSD MRI studies (2/4, continues over 4 pages) ns = not stated ns = not stated/ not recruited. Rows in BOLD indicate studies included in the PTSD region-of-interest meta-analysis, rows in italics indicate studies included in the VBM meta-analysis, rows in both BOLD and italics indicate studies included in both the region-of-interest and VBM meta-analyses, rows in normal typeface were not included in either meta-analysis.

Table S1. Database of PTSD MRI studies (continued)					
Study	No. of PTSD Patients	No. Non-Traumatised Controls (NTC)	No. Traumatised Controls (TC)	Diagnostic Criteria	Mean Patient Age, y
Weniger et al (2008)	10	25	ns	DSM-IV	32
Schuff et al (2008)	55	49	ns	DSM-IV	48.9
Bryant et al (2008)	13	13	13	CAPS	ns
<i>Carrion et al (2009)</i>	24	24	<i>ns</i>	<i>DSM-IV</i>	<i>11</i>
Felmingham et al (2009)	21	ns	17	CIDI	ns
Looi et al (2009)	19	ns	17	DSM-IV	ns
Rogers et al (2009)	9	ns	16	CAPS	44.56
Woodward et al (2009)	50	ns	47	DSM-IV	ns
Chen et al (2009)	12	ns	12	DSM-IV	34.56
Carrion et al (2010)	30	15	ns	CAPS	13.2
Landre et al (2010)	17	17	ns	DSM-IV	24.9
<i>Nardo et al (2010)</i>	21	<i>ns</i>	22	<i>DSM-IV</i>	<i>41.7</i>
Wang et al (2010)	17	ns	19	DSM-IV	41
Thomaes et al (2010)	33	30	ns	DSM-IV	35.3
Sui et al (2010)	11	12	8	DSM-IV	25.55
Sui et al (2010)	11	12	ns	DSM-IV	24.46
Hunter et al (2011)	7	11	ns	DSM-IV	57.43
Baldacara et al (2011)	42	ns	42	DSM-IV	34.91
Eckart et al (2011)	20	11	16	DSM-IV	36.1
Eckart et al (2011)	20	13	19	DSM-IV	36.2
Lyoo et al (2011)	30	36	ns	DSM-IV	27
Savitz et al (2011)	22	75	ns	DSM-IV	34.8
Schulz-Heik et al (2011)	51	ns	48	DSM-IV	49.3
Zhang et al (2011)	10	ns	10	DSM-IV	40.8
Apfel et al (2011)	41	95	64	DSM-IV	42.1
<i>Ahmed et al (2012)</i>	21	<i>ns</i>	32	<i>DSM-IV</i>	<i>16.17</i>
<i>Chao et al (2012)</i>	21	<i>ns</i>	20	<i>DSM-IV</i>	<i>35.9</i>
Chen et al (2012)	10	20	10	DSM-IV	40.8
<i>Herringa et al (2012)</i>	13	<i>ns</i>	15	<i>DSM-IV</i>	<i>28.9</i>
Morey et al (2012)	99	ns	101	DSM-IV	38.4
<i>Rocha-Rego et al (2012)</i>	16	<i>ns</i>	16	<i>DSM-IV</i>	<i>43.3</i>
Tavanti et al (2012)	25	25	ns	DSM-IV	38.16

Table S1 (Continued): Database of PTSD MRI studies (3/4, continues over 4 pages) ns = not stated/ not recruited. Rows in BOLD indicate studies included in the PTSD region-of-interest meta-analysis, rows in italics indicate studies included in the VBM meta-analysis, rows in both BOLD and italics indicate studies included in both the region-of-interest and VBM meta-analyses, rows in normal typeface were not included in either meta-analysis.

Table S1. Database of PTSD MRI studies (continued)

Study	No. of PTSD Patients	No. Non-Traumatised Controls (NTC)	No. Traumatised Controls (TC)	Diagnostic Criteria	Mean Patient Age, y
Kuo et al (2012)	42	<i>ns</i>	45	<i>DSM-IV</i>	49.5
Chao et al (2013)	39	75	43	<i>DSM-IV</i>	42.7
Jatzko et al (2013)	15	15	<i>ns</i>	<i>DSM-IV</i>	48.3
Nardo et al (2013)	15	<i>ns</i>	17	<i>DSM-IV</i>	43.33
Shu et al (2013)	11	11	<i>ns</i>	<i>DSM-IV</i>	36.3
<i>Tan et al (2013)</i>	12	<i>ns</i>	14	<i>DSM-IV</i>	37.6
Weems et al (2013)	24	24	<i>ns</i>	<i>DSM-IV</i>	10.96
Baldacara et al (2014)	32	<i>ns</i>	32	<i>DSM-IV</i>	34.8
Starcevic et al (2014)	49	<i>ns</i>	30	<i>ICD-10</i>	46.47
Zhang et al (2014)	14	25	<i>ns</i>	<i>DSM-IV</i>	33.1
Levy-Gigi et al (2015)	26	28	<i>ns</i>	<i>DSM-IV</i>	35.46
<i>Keding et al (2015)</i>	27	28	<i>ns</i>	<i>DSM-IV</i>	14.2
Chalavi et al (2015)	16	30	<i>ns</i>	<i>DSM-IV</i>	40.75
Chalavi et al (2015)	16	<i>ns</i>	25	<i>DSM-IV</i>	40.75
Starcevic et al (2015)	25	59	35	<i>ICD-10</i>	47.08
Veer et al (2015)	12	24	<i>ns</i>	<i>DSM-IV</i>	28.08
<i>Cheng et al (2015)</i>	30	27	<i>ns</i>	<i>DSM-IV</i>	26.3
Mueller et al (2015)	40	<i>ns</i>	22	<i>CAPS</i>	32.7
Cortese et al (2015)	20	<i>ns</i>	45	<i>DSM-IV</i>	30.5
Demers et al (2015)	16	<i>ns</i>	18	<i>DSM-IV</i>	34.6
<i>Nardo et al (2015)</i>	21	25	<i>ns</i>	<i>DSM-IV</i>	42.8
De Bellis et al (2015)	38	12	<i>ns</i>	<i>DSM-IV</i>	10.3
Sussman et al (2016)	23	37	<i>ns</i>	<i>DSM-IV</i>	37.3
Zandieh et al (2016)	9	<i>ns</i>	78	<i>DSM-IV</i>	38.8
Rubin et al (2016)	17	39	11	<i>DSM-IV</i>	37.5
<i>Morey et al (2016)</i>	31	57	32	<i>DSM-IV</i>	9.9
Helpman et al (2016)	41	<i>ns</i>	36	<i>DSM-IV</i>	35.895
Li et al (2016)	67	<i>ns</i>	24	<i>DSM-IV</i>	41.9
Luo et al (2016)	57	10	<i>ns</i>	<i>DSM-IV</i>	57.1

Table S1 (Continued). Database of PTSD MRI studies. (4/4, continues over 4 pages) *ns* = not stated/ not recruited. Rows in BOLD indicate studies included in the PTSD region-of-interest meta-analysis, rows in italics indicate studies included in the VBM meta-analysis, rows in both BOLD and italics indicate studies included in both the region-of-interest and VBM meta-analyses, rows in normal typeface were not included in either meta-analysis.

Table S2. Meta-analysis Comparing Patients with PTSD vs Non-traumatised-controls (NTC)											
		Comparison of PTSD patients and NTC						Heterogeneity		S.S. Bias	Leave-one-out
Region	No. of studies	Effect size	95% CI			Effect size p-value	Size vs Control, %	I ² (%)	p-value	p-value	% effect sizes, p<0.05
CSF (total)	5	-0.19	-1.12	to	0.74	0.69	99.0	87	<0.01	0.93	-
Brain (total)	16	-0.23	-0.39	to	-0.07	<0.01	98.2	0	0.57	0.07	100
White Matter (total)	7	0.03	-0.35	to	0.40	0.89	100.0	52	0.05	0.00	-
Gray Matter (total)	7	-0.47	-0.83	to	-0.11	0.01	96.2	46	0.08	0.86	86
Intracranial Volume (total)	6	-0.14	-0.44	to	0.16	0.36	98.4	0	0.47	0.48	-
Insula (total)	4	-0.84	-1.11	to	-0.56	<0.01*	93.7	0	0.63	0.08	100
Insula (right)	3	-0.53	-0.89	to	-0.16	<0.01	95.1	0	0.73	-	67
Insula (left)	3	-0.78	-1.29	to	-0.28	<0.01	93.0	43	0.18	-	67
Anterior Cingulate (total)	4	-0.10	-0.50	to	0.29	0.61	97.8	18	0.30	-	-
Anterior Cingulate (right)	4	-0.04	-0.52	to	0.45	0.88	98.5	44	0.15	-	-
Anterior Cingulate (left)	4	-0.18	-0.54	to	0.17	0.31	97.3	0	0.54	-	-
Rostral Anterior Cingulate (total)	3	-0.23	-0.72	to	0.27	0.37	97.0	68	0.05	-	-
Caudate (total)	3	-0.06	-0.42	to	0.30	0.75	99.5	0	0.43	-	-
Caudate (right)	3	-0.07	-0.43	to	0.29	0.69	99.2	0	0.52	-	-
Caudate (left)	3	-0.05	-0.41	to	0.31	0.78	99.5	0	0.41	-	-
Temporal Lobe (total)	5	-0.21	-0.61	to	0.20	0.31	98.0	47	0.11	0.33	-
Temporal Lobe (right)	4	-0.25	-0.60	to	0.11	0.17	97.2	23	0.27	-	-
Temporal Lobe (left)	4	-0.06	-0.67	to	0.54	0.84	100.1	73	0.01	-	-
Parahippocampal Gyrus (total)	3	-0.37	-0.68	to	-0.06	0.02	96.0	0	0.44	-	33
Hippocampus (total)	30	-0.60	-0.79	to	-0.41	<0.01*	92.4	53	<0.01	0.39	100
Hippocampus (right)	28	-0.52	-0.71	to	-0.32	<0.01	92.7	51	<0.01	0.05	100
Hippocampus (left)	28	-0.49	-0.69	to	-0.29	<0.01	92.7	52	<0.01	0.14	100
Amygdala (total)	13	-0.26	-0.57	to	0.05	0.11	96.1	66	<0.01	0.76	-
Amygdala (right)	12	-0.22	-0.57	to	0.14	0.23	95.8	68	<0.01	0.43	-
Amygdala (left)	12	-0.25	-0.61	to	0.10	0.16	95.6	68	<0.01	0.62	-
Corpus Callosum (total)	4	-0.36	-0.99	to	0.27	0.26	95.2	70	0.02	-	-

Table S2. Meta-analysis of regional brain volumes comparing patients with post-traumatic stress disorder to non-trauma exposed controls. Bold indicates significant differences. S.S Bias = Small Study Bias, CI = confidence interval, Non-traumatised-controls = healthy non-trauma-exposed controls. *Result remained significant after Bonferroni correction for multiple comparisons of 26 brain structures. Leave-one-out analysis examines if the pooled effect size becomes non-significant when removing one effect size at a time; a value of 100% which is the most robust result indicates that the pooled effect size remains significant when 100% of effect sizes are removed in turn.

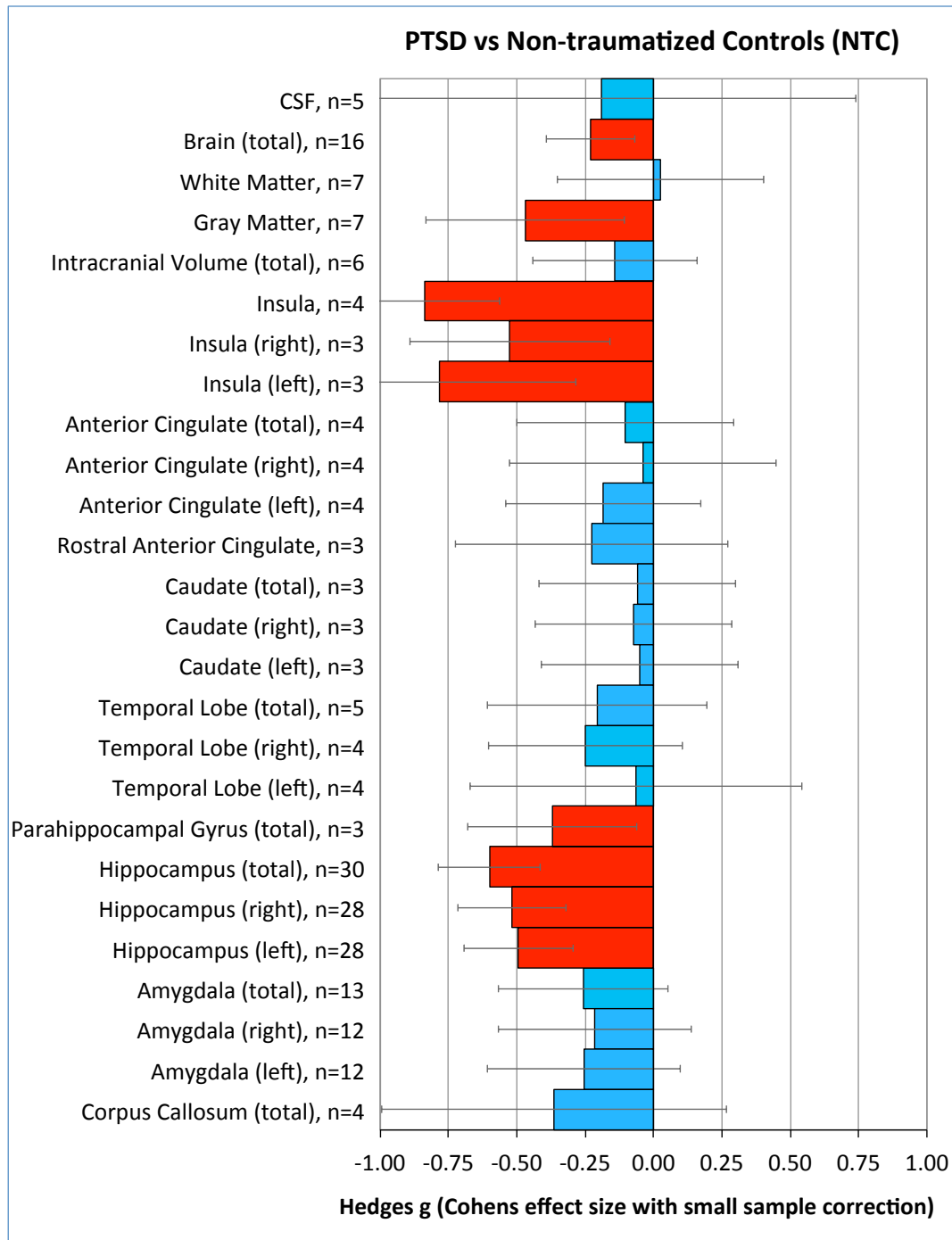


Figure S2. Meta-analysis of regional brain volumes comparing patients with post-traumatic stress disorder to non-traumatized control group. Hedges g (Cohen effect size with small sample correction) is shown for each structure, with 95% confidence intervals. The effect size is positive when the structure is larger in patients with PTSD compared with controls and negative when the structure is smaller in PTSD patients. Red indicates significant differences. The number of studies included in each meta-analysis is indicated with each structure. Non-traumatized-controls = healthy non-trauma exposed controls.

Table S3. Meta-analysis of Comparing Patients with PTSD vs Traumatised-controls (TC)											
		Comparison of PTSD patients and TC						Heterogeneity		S.S. Bias	Leave-one-out
Region	No. of studies	Effect size	95% CI			Effect size p-value	Size vs Control, %	I2 (%)	p-value	p-value	% effect sizes, p<0.05
CSF (total)	3	0.01	-0.43	to	0.45	0.96	100.0	0	0.70	-	-
Brain (total)	12	-0.24	-0.44	to	-0.03	0.02	97.9	13	0.31	0.89	83
White Matter (total)	4	-0.23	-0.58	to	0.11	0.19	97.8	0	0.92	-	-
Superior Frontal Gyrus (total)	3	-0.52	-0.81	to	-0.24	<0.01*	94.7	14	0.31	-	100
Gray Matter (total)	5	-0.04	-0.54	to	0.46	0.86	99.5	55	0.07	0.18	-
Intracranial Volume (total)	10	-0.24	-0.46	to	-0.02	0.030	97.4	15	0.29	0.18	60
Entorhinal Cortex (total)	3	-0.04	-0.31	to	0.22	0.742	98.9	0	0.37	-	-
Insula (total)	3	-0.46	-0.73	to	-0.19	<0.01*	97.5	0	0.71	-	-
Pars Orbitalis IFG (total)	3	-0.19	-0.42	to	0.05	0.118	98.7	0	0.74	-	-
Anterior Cingulate (total)	5	-0.49	-0.78	to	-0.20	<0.01*	92.4	40	0.14	0.96	100
Rostral Anterior Cingulate (total)	3	-0.11	-0.42	to	0.19	0.46	98.0	18	0.30	-	-
Isthmus Anterior Cingulate (total)	3	-0.09	-0.53	to	0.36	0.70	99.2	67	0.05	-	-
Orbitofrontal Cortex, lateral (total)	3	-0.35	-0.59	to	-0.12	<0.01	98.0	0	0.97	-	100
Parahippocampal Gyrus (total)	6	0.06	-0.42	to	0.55	0.80	101.1	81	<0.01	0.17	-
Parahippocampal Gyrus (right)	3	0.43	0.02	to	0.83	0.04	108.2	12	0.32	-	33
Parahippocampal Gyrus (left)	3	0.43	0.06	to	0.80	0.02	108.1	0	0.64	-	67
Hippocampus (total)	25	-0.24	-0.42	to	-0.06	<0.01	97.2	55	<0.01	0.16	100
Hippocampus (right)	23	-0.22	-0.40	to	-0.03	0.020	97.4	49	<0.01	0.09	100
Hippocampus (left)	23	-0.17	-0.37	to	0.03	0.094	97.2	56	<0.01	0.05	-
Amygdala (total)	15	-0.11	-0.39	to	0.16	0.42	98.5	75	<0.01	0.59	-
Amygdala (right)	13	-0.13	-0.44	to	0.18	0.41	98.3	76	<0.01	0.37	-
Amygdala (left)	13	-0.14	-0.46	to	0.18	0.39	98.0	77	<0.01	0.86	-

Table S3. Meta-analysis of regional brain volumes comparing patients with post-traumatic stress disorder to trauma-exposed without PTSD. Bold indicates significant differences. S.S Bias = Small Study Bias, CI = confidence interval, Non-traumatized-controls = healthy non-trauma exposed controls. *Result remained significant after Bonferroni correction for multiple comparisons of 22 brain structures. Leave-one-out analysis examines if the pooled effect size becomes non-significant when removing one effect size at a time; a value of 100% which is the most robust result indicates that the pooled effect size remains significant when 100% of effect sizes are removed in turn.

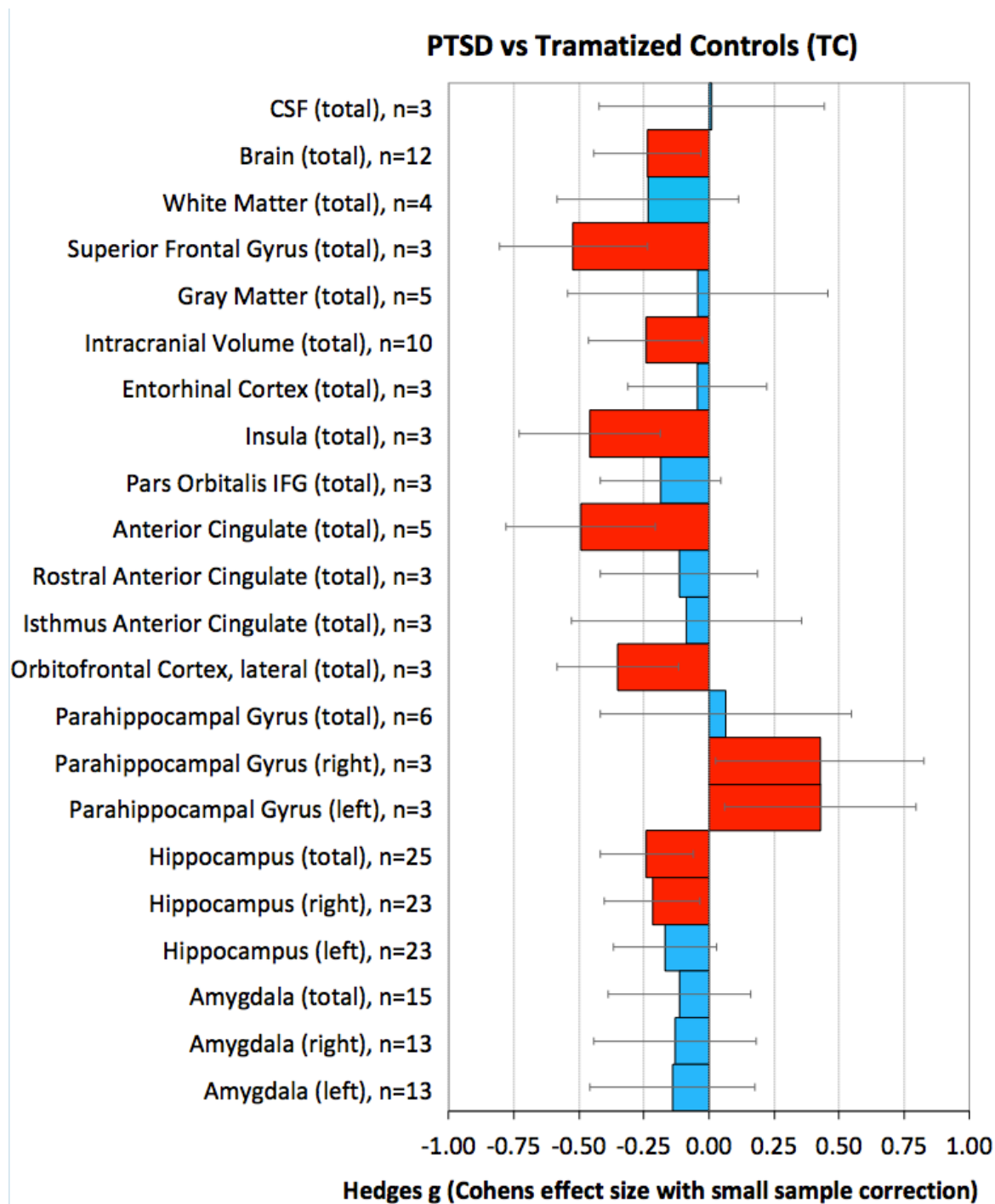


Figure S3. Meta-analysis of regional brain volumes comparing patients with post-traumatic stress disorder to trauma-exposed without PTSD. Hedges g (Cohen effect size with small sample correction) is shown for each structure, with 95% confidence intervals. The effect size is positive when the structure is larger in patients with PTSD compared with controls and negative when the structure is smaller in PTSD patients. Red indicates significant differences. The number of studies included in each meta-analysis is indicated with each structure. Traumatized-controls = exposed to trauma but without PTSD.

Table S4. Meta-analysis Comparing Traumatised-controls (TC) vs Non-traumatised-controls (NTC)											
		Comparison of TC and NTC						Heterogeneity		S.S. Bias	Leave-one-out
Region	No. of studies	Effect size		95% CI		Effect size		Size vs Control,%	I2 (%)	p-value	% effect sizes, p<0.05
						p-value					
Brain (total)	7	0.03	-0.23	to	0.29	0.84	100.1	0	0.88	0.17	-
Intracranial Volume (total)	3	-0.21	-1.14	to	0.71	0.65	98.6	72	0.03	-	-
Hippocampus (total)	13	-0.37	-0.55	to	-0.19	<0.01*	96.1	5	0.40	0.97	100
Hippocampus (right)	12	-0.35	-0.60	to	-0.10	<0.01	95.4	35	0.11	0.40	100
Hippocampus (left)	12	-0.35	-0.54	to	-0.15	<0.01*	95.6	0	0.52	0.16	100
Amygdala (total)	6	-0.15	-0.48	to	0.18	0.366	98.9	48	0.09	0.86	-
Amygdala (right)	5	0.07	-0.35	to	0.49	0.74	101.6	50	0.09	0.57	-
Amygdala (left)	5	-0.10	-0.40	to	0.20	0.51	99.4	12	0.34	0.59	-

Table S4. Meta-analysis of regional brain volumes comparing trauma-exposed without PTSD to healthy controls. Bold indicates significant differences. S.S Bias = Small Study Bias, CI = confidence interval, Traumatized-controls = exposed to trauma but without PTSD; Non-traumatized-controls = healthy non-trauma exposed controls. *Result remained significant after Bonferroni correction for multiple comparisons of 8 brain structures. Leave-one-out analysis examines if the pooled effect size becomes non-significant when removing one effect size at a time; a value of 100% which is the most robust result indicates that the pooled effect size remains significant when 100% of effect sizes are removed in turn.

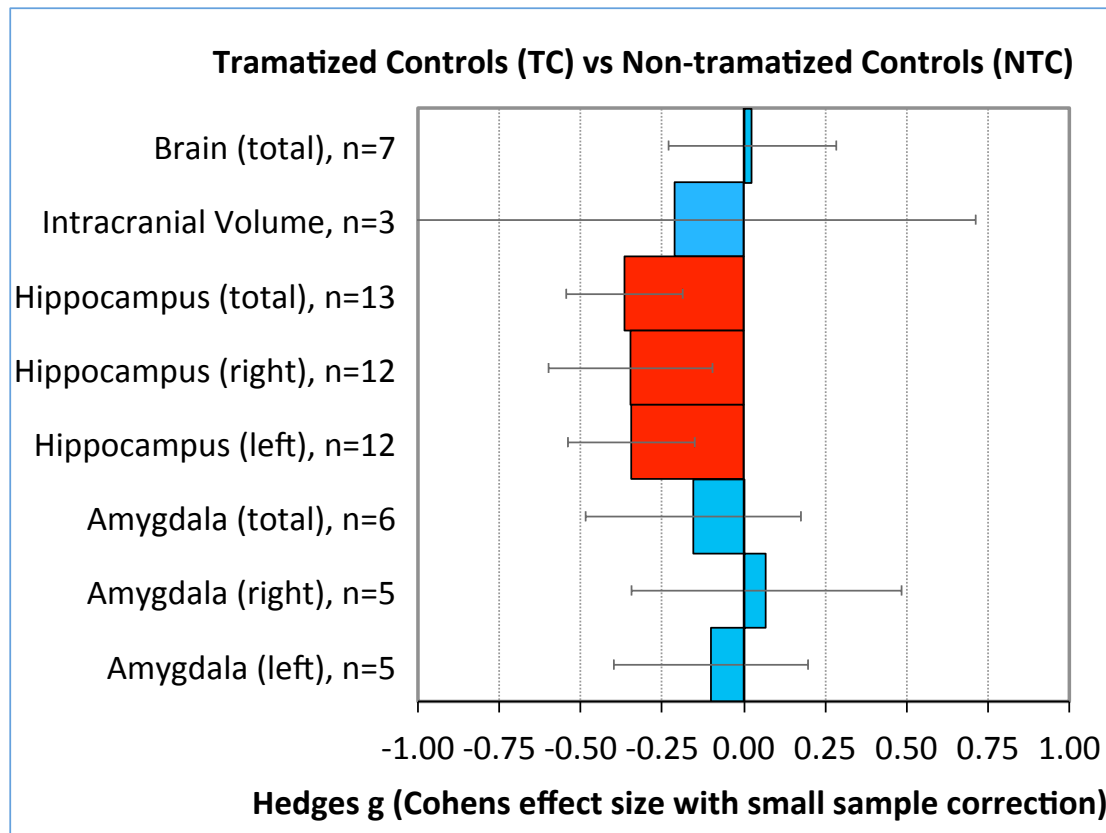


Figure S4. Meta-analysis of regional brain volumes comparing trauma-exposed without PTSD to healthy controls. Hedges g (Cohen effect size with small sample correction) is shown for each structure, with 95% confidence intervals. The effect size is positive when the structure is larger in patients with PTSD compared with controls and negative when the structure is smaller in PTSD patients. Red indicates significant differences. The number of studies included in each meta-analysis is indicated with each structure. Traumatized-controls = exposed to trauma but without PTSD; Non-traumatized-controls = healthy non-trauma exposed controls.

			Comparison of PTSD patients and all controls						Heterogeneity			S.S. Bias
Region	No. of studies	No. of PTSD/Ctrls	Effect size	95% CI		Effect size p-value	Size vs Controls, %		Q	I ² (%)	p-value	p-value
Lateral Ventricles (total)	3	79/135	0.20	-0.09	to 0.48	0.17	109.0		1.3	0	0.52	-
Brain (total)	22	422/500	-0.30	-0.46	to -0.15	<0.01*	97.4		25.5	18	0.23	0.27
Cerebellum (total)	3	138/199	-0.57	-0.80	to -0.35	<0.01*	94.4		1.5	0	0.47	-
Intracranial Volume (total)	15	282/348	-0.33	-0.51	to -0.15	<0.01*	96.6		22.5	25	0.16	1.00
Frontal Lobe (total)	3	110/171	-0.48	-0.72	to -0.23	<0.01*	94.1		1.8	0	0.41	-
Prefrontal Cortex (total)	3	121/157	-0.32	-0.74	to 0.09	0.13	95.0		5.5	64	0.06	-
Gray Matter (total)	13	297/374	-0.42	-0.68	to -0.16	<0.01	96.2		27.5	56	<0.01	0.92
Insula (total)	6	161/216	-0.58	-0.89	to -0.28	<0.01*	96.1		9.6	48	0.09	0.69
Insula (right)	4	82/96	-0.35	-0.69	to -0.02	0.04	97.0		3.6	17	0.31	-
Insula (left)	4	82/96	-0.61	-1.09	to -0.13	0.01	95.1		7.0	57	0.07	-
Cerebellar Gray Matter (total)	3	73/100	-0.38	-0.80	to 0.04	0.08	95.7		3.4	40	0.19	-
Cerebral Volume (total)	4	168/244	-0.48	-0.70	to -0.26	<0.01*	95.7		6.6	10	0.36	-
Superior Temporal Gyrus (total)	6	162/192	-0.15	-0.48	to 0.19	0.39	98.6		11.5	57	0.04	0.89
Superior Temporal Gyrus (right)	5	122/147	-0.07	-0.47	to 0.34	0.75	99.4		10.4	61	0.03	0.63
Superior Temporal Gyrus (left)	5	122/147	-0.21	-0.64	to 0.23	0.35	97.7		11.5	65	0.02	0.92
Anterior Cingulate (total)	11	279/367	-0.30	-0.58	to -0.01	0.041	95.7		31.5	65	<0.01	0.52
Anterior Cingulate (right)	8	191/238	-0.09	-0.31	to 0.13	0.43	98.4		10.0	20	0.27	0.49
Anterior Cingulate (left)	8	191/238	-0.26	-0.55	to 0.04	0.09	94.6		16.7	52	0.03	0.79
Putamen (total)	5	172/250	0.10	-0.10	to 0.29	0.33	100.7		3.9	0	0.42	0.13
Putamen (right)	5	172/250	0.14	-0.06	to 0.34	0.17	101.3		4.0	0	0.41	0.02
Putamen (left)	5	172/250	0.05	-0.15	to 0.25	0.62	100.0		3.9	0	0.42	0.34
Caudate (total)	7	217/287	-0.02	-0.21	to 0.18	0.88	99.9		6.9	13	0.33	0.48
Caudate (right)	7	217/287	0.00	-0.20	to 0.20	0.99	100.2		7.0	14	0.32	0.58
Caudate (left)	7	217/287	-0.04	-0.22	to 0.14	0.66	99.4		6.0	1	0.42	0.42
Temporal Lobe (total)	8	187/245	-0.42	-0.69	to -0.15	<0.01	95.5		12.1	42	0.10	0.46
Temporal Lobe (right)	7	178/236	-0.44	-0.66	to -0.21	<0.01*	95.1		7.4	19	0.29	0.32
Temporal Lobe (left)	7	178/236	-0.29	-0.64	to 0.05	0.09	96.8		16.5	64	0.01	0.08
Hippocampus (total)	47	1066/1240	-0.43	-0.57	to -0.29	<0.01*	94.9		109.8	58	<0.01	<0.01
Hippocampus (right)	43	932/1067	-0.38	-0.52	to -0.24	<0.01*	95.1		91.0	54	<0.01	<0.01
Hippocampus (left)	43	932/1067	-0.34	-0.48	to -0.20	<0.01*	95.3		91.2	54	<0.01	0.02
Amygdala (total)	28	759/925	-0.25	-0.43	to -0.06	<0.01	96.4		84.6	68	<0.01	0.58
Amygdala (right)	25	656/781	-0.22	-0.43	to -0.01	0.04	96.3		78.6	69	<0.01	0.83
Amygdala (left)	25	656/781	-0.26	-0.47	to -0.05	0.02	95.8		83.5	71	<0.01	0.41
Vermis (total)	5	180/245	-0.63	-1.12	to -0.14	0.01	91.5		21.6	82	<0.01	0.42
Corpus Callosum (total)	7	183/289	-0.34	-0.72	to 0.03	0.07	95.1		19.2	69	<0.01	0.30
Corpus Callosum, rostrum	3	82/141	-0.16	-0.44	to 0.11	0.25	95.3		1.8	0	0.41	-
Corpus Callosum, genu	3	82/141	-0.41	-0.84	to 0.02	0.06	91.6		2.8	29	0.24	-
Corpus Callosum, rostral body	3	82/141	-0.18	-0.46	to 0.09	0.19	95.9		1.6	0	0.44	-
Corpus Callosum, anterior midbody	3	82/141	-0.50	-0.78	to -0.22	<0.01*	90.7		0.4	0	0.82	-
Corpus Callosum, posterior midbody	3	82/141	-0.61	-0.96	to -0.26	<0.01	87.0		2.3	12	0.32	-
Corpus Callosum, isthmus	3	82/141	-0.56	-1.07	to -0.04	0.03	88.5		3.5	43	0.17	-
Corpus Callosum, splenium	3	82/141	-0.33	-0.92	to 0.25	0.26	94.4		4.5	56	0.11	-

Table S5. Meta-analysis of regional brain volumes (including paediatric samples) comparing patients with post-traumatic stress disorder to controls. Brain regions are shown where pediatric data changes the effect size given in table 2. **Bold** indicates significant differences. S.S Bias = Small Study Bias. *Result remained significant after Bonferroni correction for multiple comparisons for 42 brain structures.

PTSD vs All controls (includes pediatric samples) [1/2]

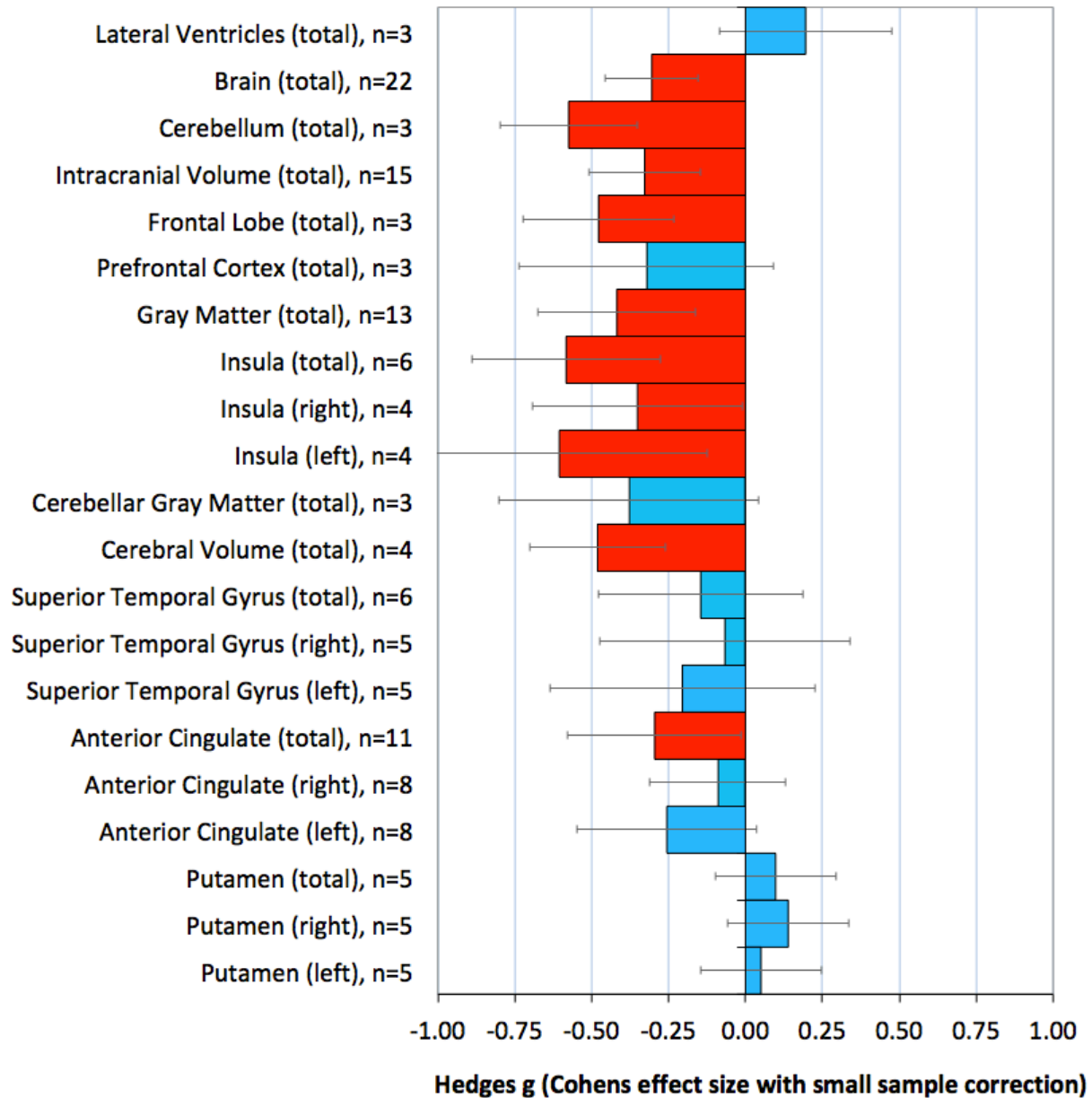


Figure S5a. Meta-analysis of regional brain volumes (including paediatric samples) comparing patients with post-traumatic stress disorder to controls. Hedges *g* (Cohen effect size with small sample correction) is shown for each structure, with 95% confidence intervals. The effect size is positive when the structure is larger in patients with PTSD compared with controls and negative when the structure is smaller in PTSD patients. Red indicates significant differences. The number of studies included in each meta-analysis is indicated for each structure.

PTSD vs All controls (includes pediatric samples) [2/2]

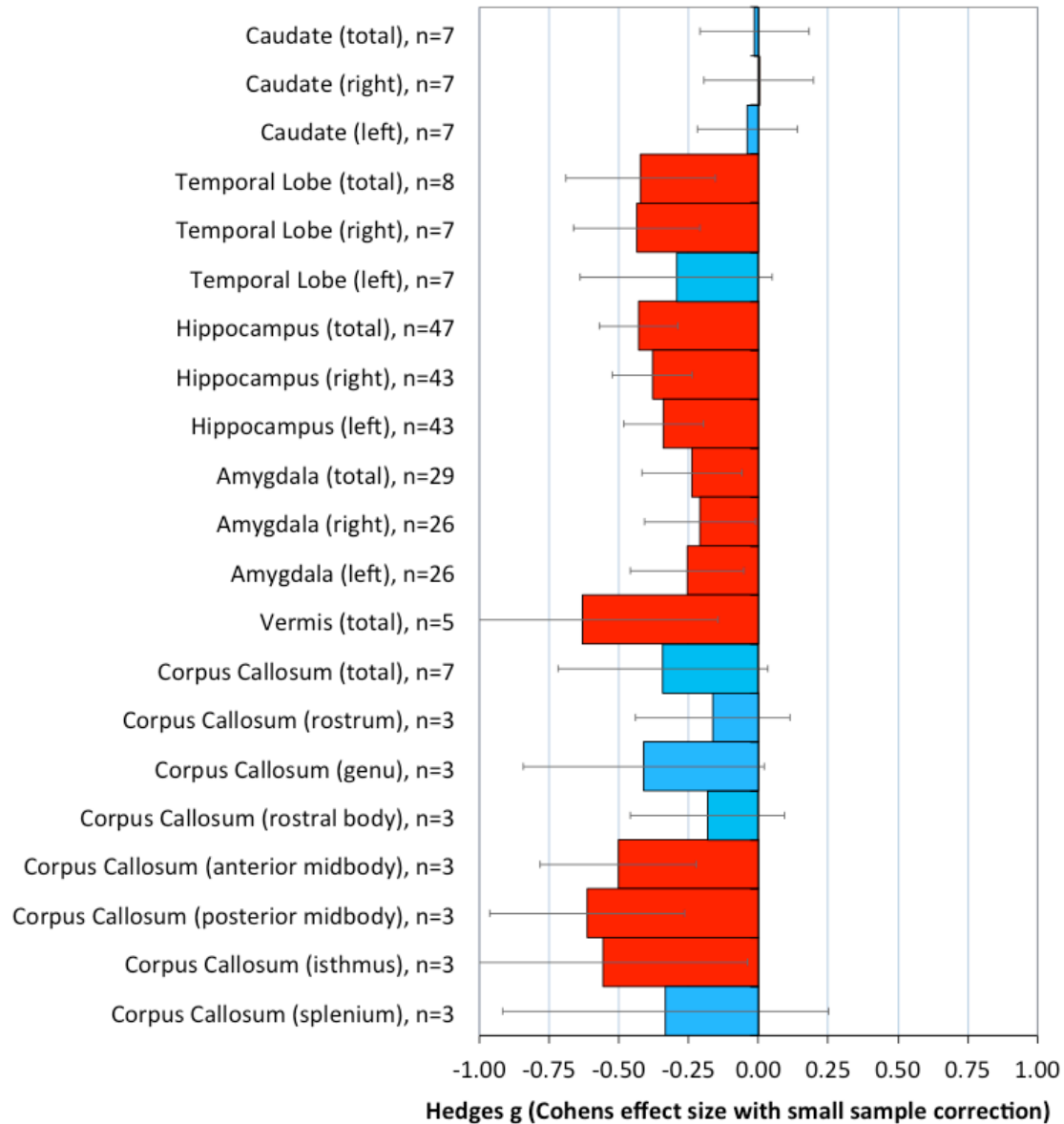


Figure S5b. Meta-analysis of regional brain volumes (including paediatric samples) comparing patients with post-traumatic stress disorder to controls. Hedges g (Cohen effect size with small sample correction) is shown for each structure, with 95% confidence intervals. The effect size is positive when the structure is larger in patients with PTSD compared with controls and negative when the structure is smaller in PTSD patients. Red indicates significant differences. The number of studies included in each meta-analysis is indicated for each structure.

Table S6. Meta-analysis Comparing Patients with PTSD vs non-traumatised-controls (NTC), (includes pediatric samples)											
		Comparison of PTSD patients and NTC						Heterogeneity			S.S. Bias
Region	No. of studies	Effect size	95% CI			Effect size p-value	Size vs Control %	Q	I ² (%)	p-value	p-value
Lateral Ventricles (total)	3	0.20	-0.09	to	0.48	0.17	109.0	1	0	0.52	-
Brain (total)	17	-0.28	-0.45	to	-0.12	<0.01*	97.5	18	12	0.31	0.14
Gray Matter (total)	10	-0.52	-0.75	to	-0.29	<0.01*	95.4	14	35	0.13	0.20
Cerebellar Gray Matter (total)	3	-0.38	-0.80	to	0.04	0.08	95.7	3	40	0.19	-
Intracranial Volume (total)	7	-0.31	-0.62	to	-0.01	0.05	96.8	10	0	0.47	0.48
Caudate (total)	5	-0.13	-0.36	to	0.10	0.26	98.1	3	0	0.64	0.32
Caudate (right)	5	-0.13	-0.36	to	0.10	0.26	98.2	2	0	0.79	0.34
Caudate (left)	5	-0.13	-0.36	to	0.10	0.27	98.0	3	0	0.52	0.33
Temporal Lobe (total)	8	-0.42	-0.69	to	-0.15	<0.01*	95.5	12	42	0.10	0.46
Temporal Lobe (right)	7	-0.44	-0.66	to	-0.21	<0.01	95.1	7	19	0.29	0.32
Temporal Lobe (left)	7	-0.29	-0.64	to	0.05	0.09	96.8	17	64	0.01	0.08
Hippocampus (total)	35	-0.53	-0.70	to	-0.37	<0.01*	93.2	71	52	<0.01	0.16
Hippocampus (right)	32	-0.46	-0.63	to	-0.29	<0.01*	93.6	61	49	<0.01	0.02
Hippocampus (left)	32	-0.43	-0.61	to	-0.26	<0.01*	93.6	63	51	<0.01	0.07
Amygdala (total)	19	-0.25	-0.45	to	-0.05	0.02	96.2	38	52	<0.01	0.71
Amygdala (right)	17	-0.19	-0.42	to	0.04	0.10	96.1	37	57	<0.01	0.50
Amygdala (left)	17	-0.25	-0.48	to	-0.01	0.04	95.6	38	58	<0.01	0.64
Prefrontal Cortex (total)	3	-0.34	-0.74	to	0.07	0.11	94.9	5	58	0.10	-
Vermis (total)	4	-0.40	-0.73	to	-0.07	0.02	94.4	6	49	0.12	0.40
Corpus Callosum (total)	6	-0.49	-0.82	to	-0.17	<0.01	93.1	10	51	0.07	0.33
Corpus Callosum, rostrum	3	-0.16	-0.44	to	0.11	0.25	95.3	2	0	0.41	-
Corpus Callosum, genu	3	-0.41	-0.84	to	0.02	0.06	91.6	3	29	0.24	-
Corpus Callosum, rostral body	3	-0.18	-0.46	to	0.09	0.19	95.9	2	0	0.44	-
Corpus Callosum, anterior midbody	3	-0.50	-0.78	to	-0.22	<0.01*	90.7	0	0	0.82	-
Corpus Callosum, posterior midbody	3	-0.61	-0.96	to	-0.26	<0.01*	87.0	2	12	0.32	-
Corpus Callosum, isthmus	3	-0.56	-1.07	to	-0.04	0.03	88.5	4	43	0.17	-
Corpus Callosum, splenium	3	-0.33	-0.92	to	0.25	0.26	94.4	4	56	0.11	-

Table S6. Meta-analysis of regional brain volumes (including paediatric samples) comparing patients with post-traumatic stress disorder to non-traumatised controls. Brain regions are shown where pediatric data changes the effect size given in table S2. Bold indicates significant differences. S.S Bias = Small Study Bias, CI = confidence interval, Non-traumatised-controls = healthy non-trauma-exposed controls. * Result remained significant after Bonferroni correction for multiple comparisons for 27 brain structures

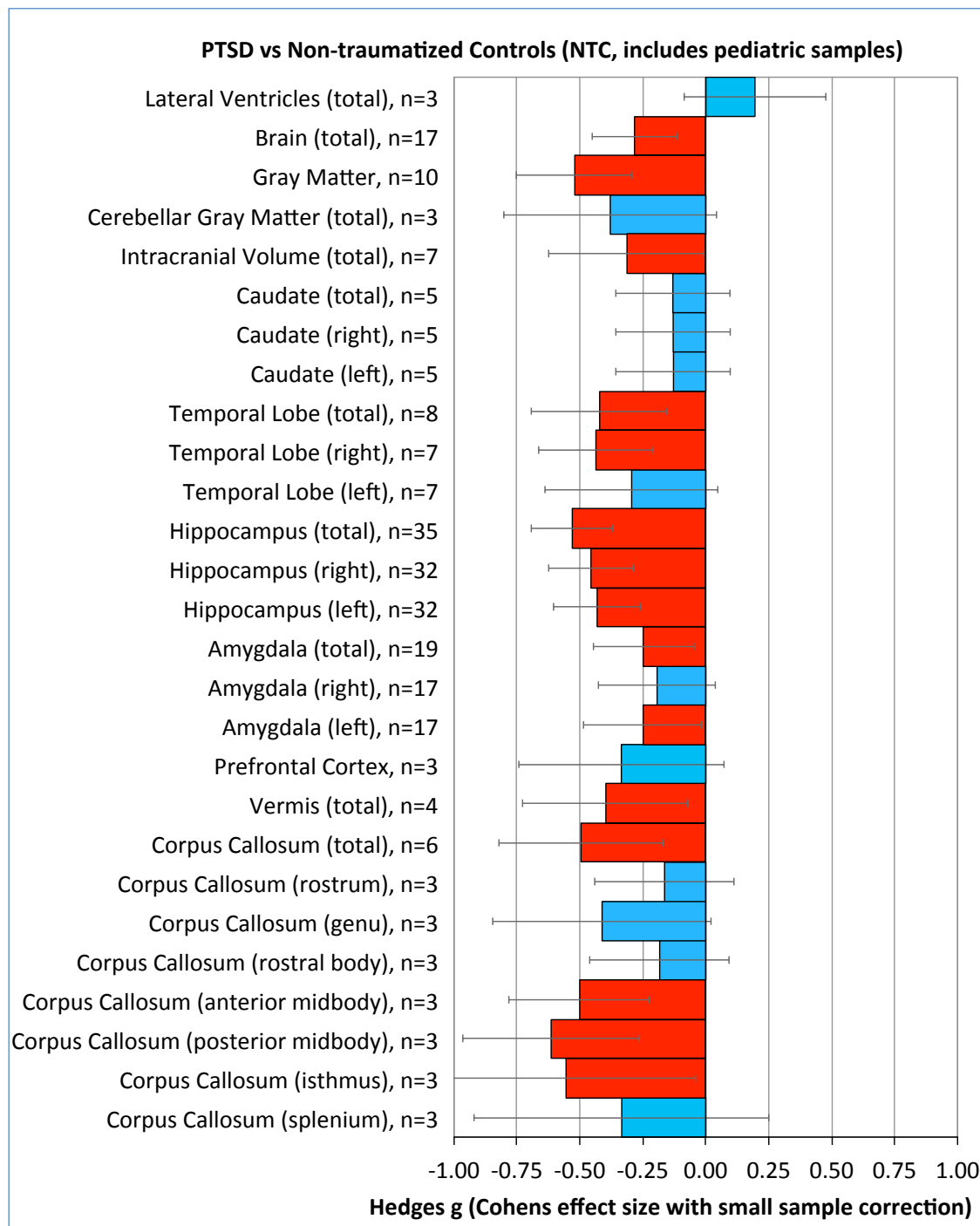


Figure S6. Meta-analysis of regional brain volumes (including paediatric samples) comparing patients with post-traumatic stress disorder to non-traumatized control group. Hedges *g* (Cohen effect size with small sample correction) is shown for each structure, with 95% confidence intervals. The effect size is positive when the structure is larger in patients with PTSD compared with controls and negative when the structure is smaller in PTSD patients. Red indicates significant differences. The number of studies included in each meta-analysis is indicated with each structure. Traumatized-controls = exposed to trauma but without PTSD.

Table S7. Meta-analysis Comparing Patients with PTSD vs Traumatised-controls (TC), (includes pediatric samples)											
		Comparison of PTSD patients and TC						Heterogeneity			S.S. Bias
Region	No. of studies	Effect size	95% CI			Effect size p-value	Size vs Control,%	Q	I2 (%)	p-value	p-value
Insula (total)	4	-0.51	-0.96	to	-0.07	0.02	96.9	9	67	0.03	-
Gray Matter (total)	5	-0.04	-0.54	to	0.46	0.86	99.5	9	55	0.07	0.18
Anterior Cingulate (total)	7	-0.34	-0.64	to	-0.04	0.03	97.6	17	59	0.02	0.84
Anterior Cingulate (right)	4	-0.13	-0.38	to	0.12	0.31	93.5	4	6	0.37	0.55
Anterior Cingulate (left)	4	-0.30	-0.76	to	0.16	0.21	97.2	14	72	<0.01	0.93
Hippocampus (total)	27	-0.25	-0.42	to	-0.08	<0.01*	97.2	56	53	<0.01	0.15
Hippocampus (right)	25	-0.23	-0.40	to	-0.06	<0.01	97.3	46	48	<0.01	0.09
Hippocampus (left)	25	-0.18	-0.36	to	0.00	0.055	97.2	52	54	<0.01	0.13
Amygdala (total)	17	-0.13	-0.38	to	0.11	0.28	98.3	57	72	<0.01	0.57
Amygdala (right)	15	-0.14	-0.40	to	0.13	0.32	98.2	51	72	<0.01	0.32
Amygdala (left)	15	-0.17	-0.45	to	0.11	0.24	97.6	55	75	<0.01	0.86

Table S7. Meta-analysis of regional brain volumes (including paediatric samples) volumes comparing patients with post-traumatic stress disorder to trauma-exposed controls without PTSD. Brain regions are shown where pediatric data changes the effect size given in table S3. Bold indicates significant differences. S.S Bias = Small Study Bias, CI = confidence interval, Non-traumatized-controls = healthy non-trauma exposed controls. *Result remained significant after Bonferroni correction for multiple comparisons for 11 brain structures

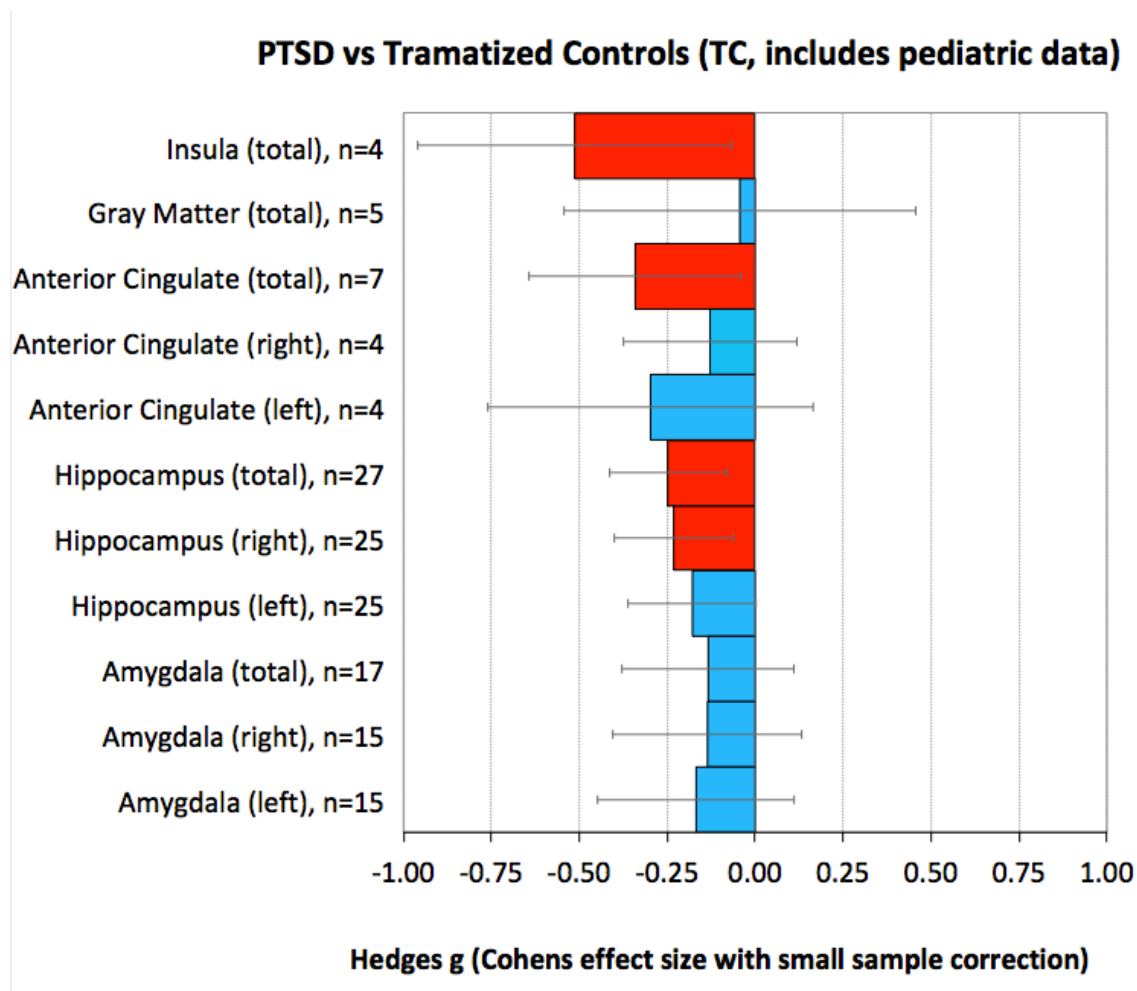


Figure S7. Meta-analysis of regional brain volumes (including paediatric samples) comparing patients with post-traumatic stress disorder to trauma-exposed without PTSD. Hedges *g* (Cohen effect size with small sample correction) is shown for each structure, with 95% confidence intervals. The effect size is positive when the structure is larger in patients with PTSD compared with controls and negative when the structure is smaller in PTSD patients. Red indicates significant differences. The number of studies included in each meta-analysis is indicated with each structure. Traumatized-controls = exposed to trauma but without PTSD.

Table S8. Statistical Comparison of the PTSD vs NTC and MDD vs controls								
	PTSD vs Control Meta-analysis			MDD vs Control Meta-analysis			PTSD vs MDD	
Region	No. of studies	Effect size	P Value	No. of studies	Effect Size	P Value	Effect Size	P Value
CSF	5	-0.19	0.69	7	0.53	0.001	-0.72	0.15
Brain	16	-0.23	0.005	25	-0.05	0.27	-0.17	0.07
Intracranial volume	6	-0.14	0.36	20	-0.12	0.056	-0.03	0.88
Gray matter	7	-0.47	0.0011	7	-0.13	0.19	-0.34	0.10
Anterior Cingulate	4	-0.10	0.61	6	-0.21	0.22	0.10	0.70
Caudate	3	-0.06	0.75	12	-0.20	0.017	0.14	0.48
Hippocampus	30	-0.60	<0.001	32	-0.48	<0.001	-0.11	0.36
Amygdala	13	-0.26	0.11	17	-0.02	0.89	-0.24	0.24

Table S8. Statistical Comparison of the present PTSD Meta-analysis With a previous Meta-analysis of Major-depressive-disorder⁴. The comparison is PTSD vs Non-traumatised-controls compared to Major-depressive-disorder vs controls. For the PTSD vs Major-depressive-disorder comparison, negative effect sizes indicate that the region is smaller in PTSD patients; positive effect sizes indicate that the region is smaller in Major-depressive-disorder patients.

Regions	MNI coordinates X, Y, Z	SDM z-value	P-value	Number of voxels	Number of studies Jackknife Sensitivity analysis
Right anterior cingulate	6, 32, 28	4.507	<0.0001	2348	13
Left superior frontal gyrus, dorsolatral	-26, 52, 20	3.425	<0.0001	763	13
Right fusiform gyrus	28, -38, -18	3.144	0.0005	86	12
Left amygdala	-28, -10, -18	2.806	0.002	58	8
Right amygdala	26, -2, -14	2.880	0.002	54	10
Left precentral gyrus	-48, 2, 42	3.078	0.0006	48	11
Right inferior temporal gyrus	56, -52, -8	2.980	0.001	28	9
Left median cingulate	-6, 16, 34	2.759	0.003	21	6
Left postcentral gyrus	-56, -6, 24	2.954	0.001	15	8
Left inferior occipital gyrus	-44, -82, -10	2.994	0.001	13	10
Left inferior frontal gyrus, triangular part	-46, 40, 6	2.781	0.003	13	7
Right inferior frontal gyrus, orbital part	28, 30, -20	2.844	0.002	12	9
Left inferior frontal gyrus, orbital part	-30, 34, -18	2.791	0.003	10	9

Table S9. Seed-based d Mapping (SDM) analysis showing decreased gray matter volumes in PTSD group compared to control group. Jackknife Sensitivity analysis demonstrates the robustness of the results, the larger the value the more consistent the result.

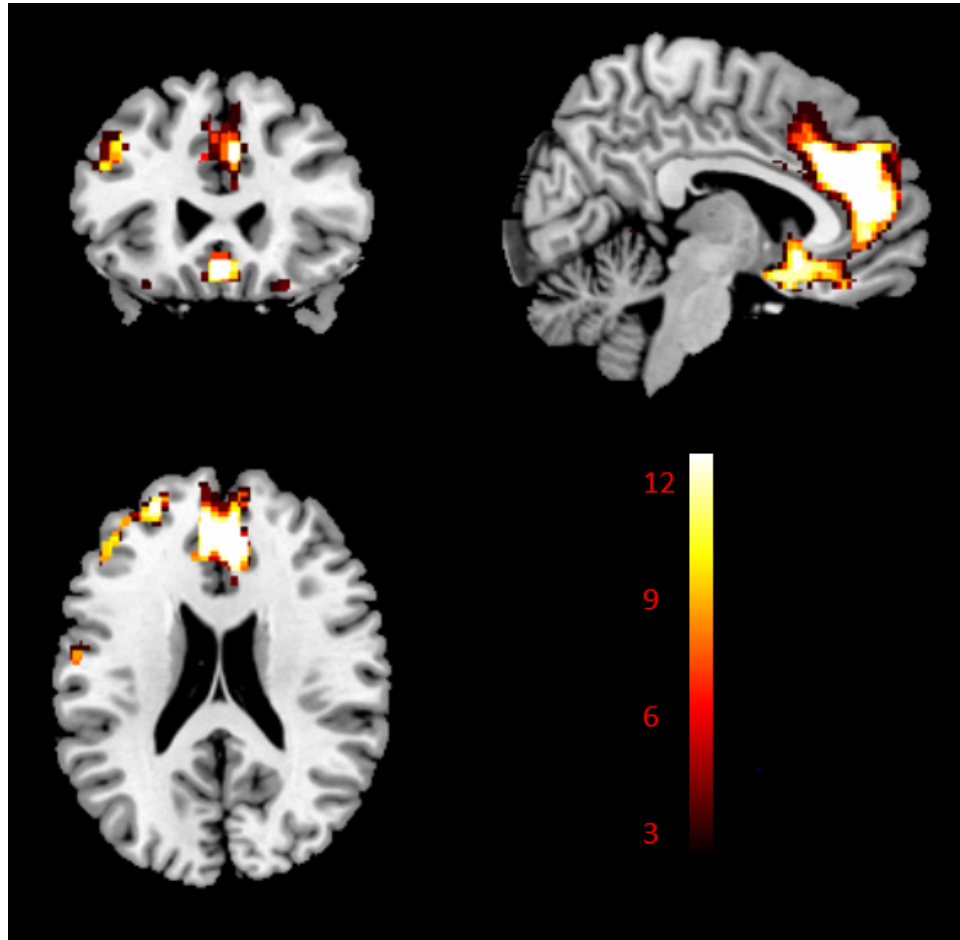


Figure S8. Binarised map of Jackknife Analyses (Main VBM Analyses). The overlaid colored regions indicate the number of sensitivity analyses reporting volume reductions in the same region. Thus the higher the value the more consistent the results.

Table S10 Regions of Significant Changes in GMV Between Patients with PTSD and NTC group – SDM Analysis					
Regions	MNI coordinates X, Y, Z	SDM z-value	P-value	Number of voxels	Number of studies in Jackknife Sensitivity analysis
Right anterior cingulate	4, 38, 22	-4.111	<0.0001	1612	5
Left precentral gyrus	-54, 2, 40	-3.420	<0.0001	391	3
Left middle frontal gyrus	-40, 32, 30	-3.397	0.0001	319	3

Table S10. Seed-based d Mapping (SDM) Analysis of 5 VBM studies showing decreased gray matter volumes in PTSD group compared to non-traumatised-control group. Jackknife Sensitivity analysis demonstrates the robustness of the results, the larger the value the more consistent the result.

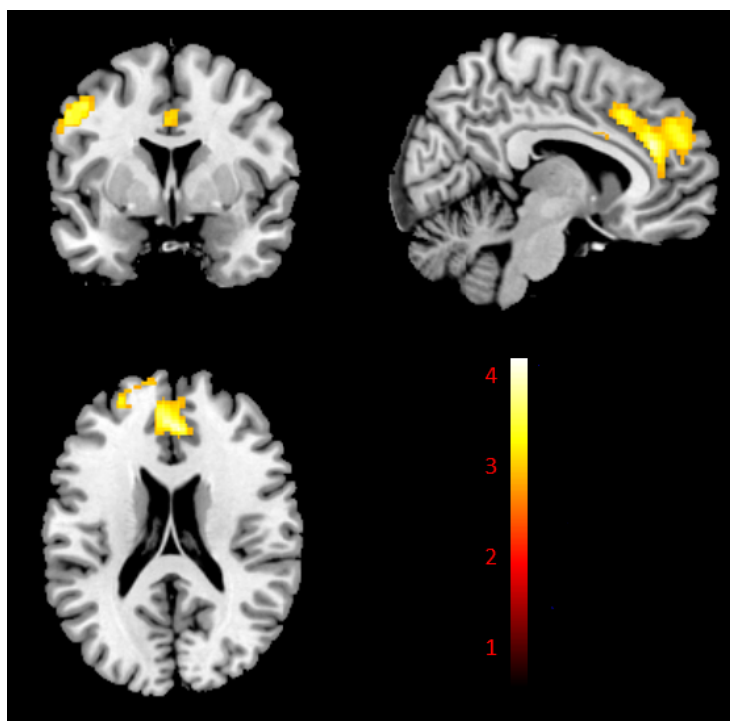


Figure S9. SDM meta-analysis of 5 VBM studies showing significant decreased gray matter volumes in PTSD group compared to non-traumatized-controls. Color bar indicates z scores. The 3D statistical map of this data is available to download.

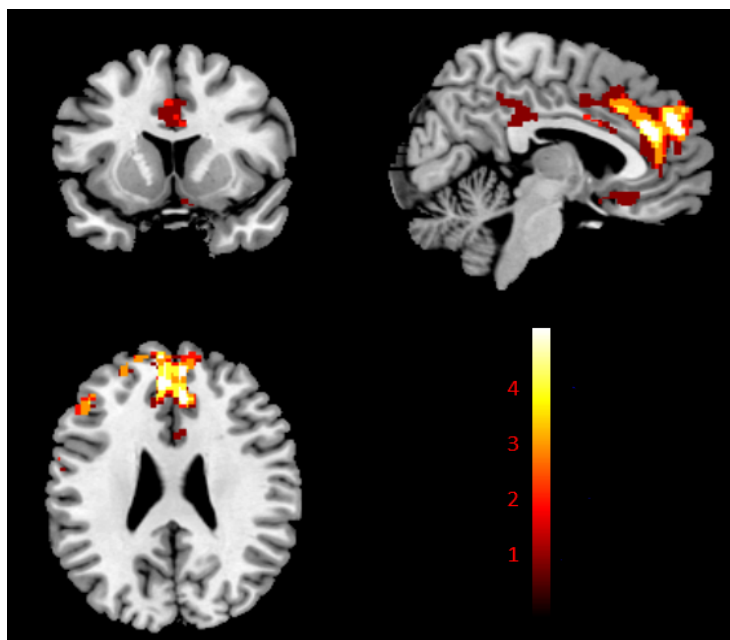


Figure S10. Binarised map of Jackknife Analyses (PTSD- Non-traumatized-controls). The overlaid coloured regions indicate the number of sensitivity analyses reporting volume reductions in the same region. Thus the higher the value the more consistent the results.

Regions	MNI coordinates X, Y, Z	SDM z-value	P-value	Number of voxels	Number of studies Jackknife Sensitivity analysis
Left insula	-34, 0, -16	-2.499	0.0004	380	8
Right superior frontal gyrus	0, 22, -12	-2.454	0.0005	214	8
Right anterior cingulate	6, 32, 28	-2.594	0.0003	137	9
Left inferior frontal gyrus	-44, 38, 8	-2.373	0.008	94	7
Left middle frontal gyrus	-32, 50, 28	-2.396	0.0007	75	7
Left middle frontal gyrus, orbital part	-38, 54, -6	-2.159	0.003	56	6
Left inferior temporal gyrus	-56, -56, -10	-2.356	0.0009	43	6
Right inferior network, inferior longitudinal fasciculus	38, -34, -14	-2.164	0.003	14	5
Right fusiform gyrus	28, -38, -18	-2.163	0.003	10	5
Left anterior cingulate	-8, 52, 2	-2.133	0.003	10	4

Table S11. Seed-based d Mapping (SDM) Analysis of 9 VBM studies showing decreased gray matter volumes in PTSD group compared to traumatised-control group. Jackknife Sensitivity analysis demonstrates the robustness of the results, the larger the value the more consistent the result.

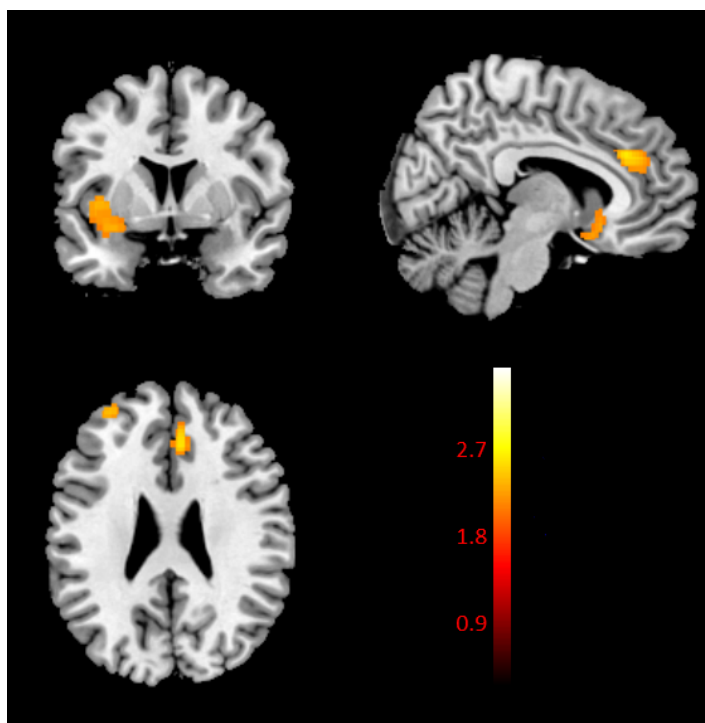


Figure S11. SDM meta-analysis of 9 VBM studies showing significant decreased gray matter volumes in PTSD group compared to Traumatized-controls. Color bar indicates z scores. The 3D statistical map of this data is available to download.

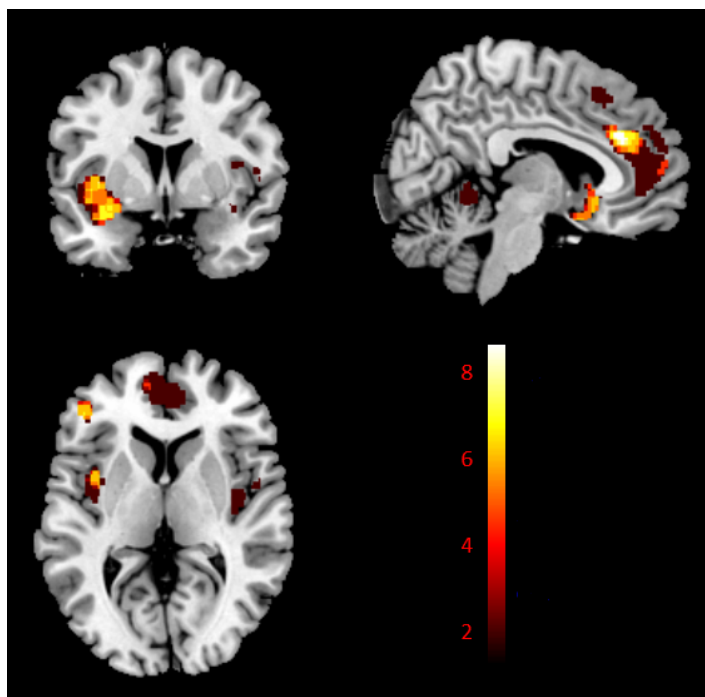


Figure S12. Binarised map of Jackknife Analyses (PTSD- Non-traumatized-controls). The overlaid colored regions indicate the number of sensitivity analyses reporting volume reductions in the same region. Thus, the higher the value the more consistent the results.

Regions	MNI coordinates X, Y, Z	SDM z-value	Number of voxels	Number of studies Jackknife Sensitivity analysis
Right anterior cingulate	6, 36, 26	-4.267	1453	17
Left superior frontal gyrus, dorsolateral	-26, 52, 20	-3.358	761	17
Right striatum	8, 14, -16	-2.732	49	13
Right median cingulate	6, -38, 40	-2.658	22	13
Right superior frontal gyrus, medial orbital	10, 66, -14	-2.733	21	14
Left precentral gyrus	-48, 0, 42	-2.757	17	13
Right inferior frontal gyrus, orbital part	28, 30, -20	-2.683	14	12
Left hippocampus	-28, -12, -20	-2.640	14	12
Right inferior temporal gyrus	54, -54, -10	-2.672	13	11
Left inferior frontal gyrus, orbital part	-34, 34, -18	-2.606	11	11

Table S12. Seed-based d Mapping (SDM) Analysis showing decreased gray matter volumes in PTSD group compared to control group. Jackknife Sensitivity analysis demonstrates the robustness of the results, the larger the value the more consistent the result.

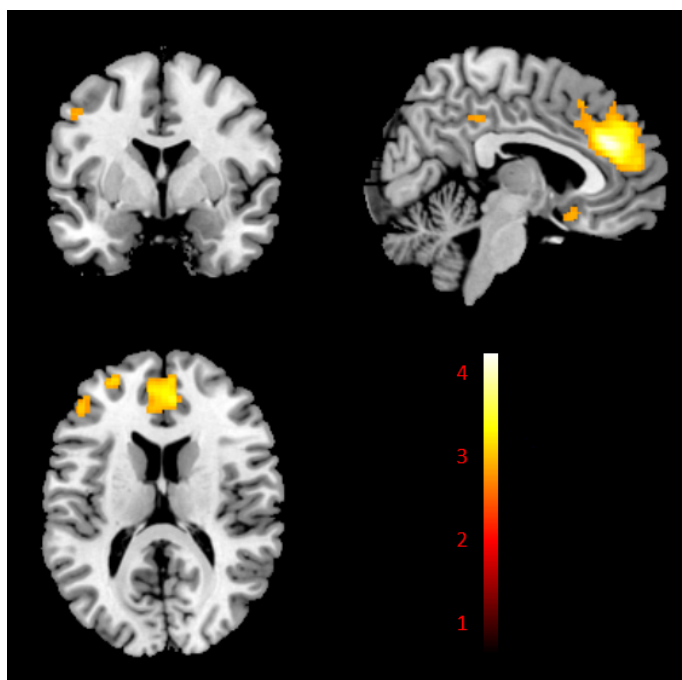


Figure S13. SDM meta-analysis of 17 VBM studies showing significant decreased gray matter volumes in PTSD group compared to all controls (including pediatric data). Color bar indicates z scores. The 3D statistical map of this data is available to download.

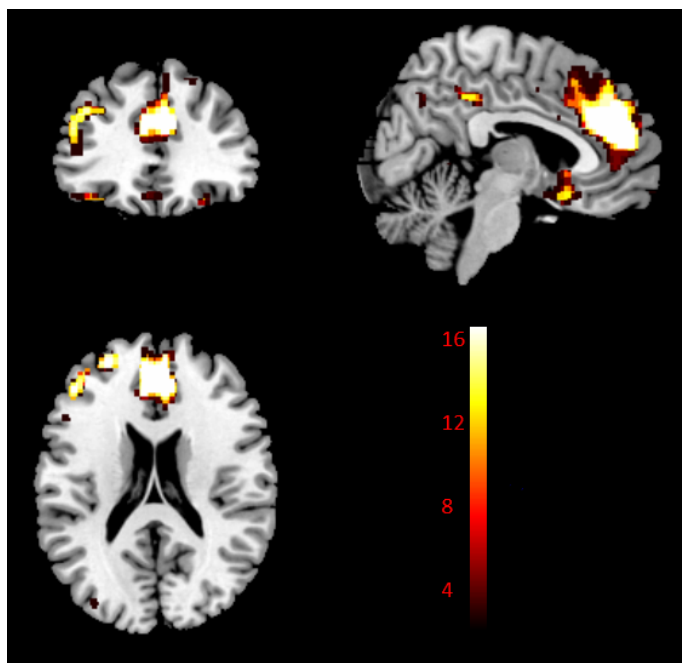


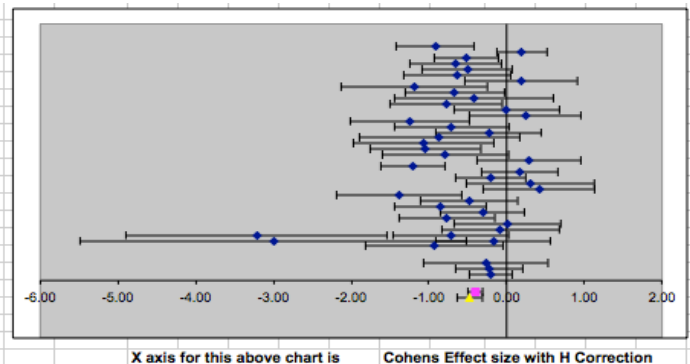
Figure S14. Binarised map of Jackknife Analyses (PTSD vs all controls – including pediatric data). The overlaid colored regions indicate the number of sensitivity analyses reporting volume reductions in the same region. Thus the higher the value the more consistent the results.

Region	Number of ROI studies (from table 2)	Hedges g ROI meta-analysis (from table 2)	Number of VBM studies	Hedges g Extracted region from VBM meta-analysis
R Insula	3	-0.53 (-0.89 to -0.16)	13	-0.11 (-0.31 to 0.10)
L Insula	3	-0.78 (-1.29 to -0.28)	13	-0.14 (-0.34 to 0.07)
R Anterior Cingulate	6	-0.14 (-0.43 to 0.14)	13	-0.28 (-0.48 to -0.07)
L Anterior Cingulate	6	-0.40 (-0.69 to -0.11)	13	-0.28 (-0.51 to -0.05)
R Hippocampus	38	-0.42 (-0.59 to -0.26)	13	-0.13 (-0.31 to 0.06)
L Hippocampus	38	-0.38 (-0.55 to -0.22)	13	-0.15 (-0.33 to 0.04)
R Amygdala	19	-0.24 (-0.52 to 0.03)	13	-0.20 (-0.38 to -0.02)
L Amygdala	19	-0.28 (-0.57 to 0.00)	13	-0.20 (-0.38 to -0.02)

Table S13. Region of interest meta-analysis compared to VBM meta-analysis (Seed-based d Mapping (SDM)). When comparing the methodologies it is important to note that effect sizes are calculated differently in each method. For example the inclusion of coordinates results in the SDM meta-analysis tends to reduce the magnitude of effect sizes as non-significant findings are assumed to be zero, furthermore SDM calculates the average effect size of a number of voxels rather than effect size of a single region. Note that the right column of this table is different from the clusters shown in table S11. In this table effect sizes are given for an entire structure, while table S11 shows clusters or ‘hot spots’ within a structure. Thus while a significant small cluster was found in the left hippocampus in table S11, when the entire structure was considered there was no overall difference in volume.

First Author	Year	Link to paper	Number of Patients (PTSD)	Number of Controls (NTC unless only a TC group is present)	Diagnosis	CAPS scores	Regions measured	Age patients	SD Age patients	Age Controls	SD Age Controls	Female patients	Female controls
Bremner JD	1995	http://ajp.r	26	22	DSM-III-R	ns	left hippocampus, right hippocampus, left ten	46	1.8	44.5	7.3	0	0
Gurvits TV	1996	http://dx.d	7	8	DSM-III-R	70.3	intracranial cravity, whole brain, subarachnoi	44.4	1.7	38.1	10	0	0
Bremner JD	1997	http://dx.d	17	17	DSM-III-R	ns	left hippocampus, right hippocampus, left ten	40.1	5.7	42.4	7.3	5	5
De_Bellis MD	1999	http://dx.d	44	61	DSM-III-R	ns	intracranial volume, cerebral volume, cortical	12.2	2.4	12	2.3	19	25
Bonne O	2001	http://ajp.r	10	27	DSM-IV	57.9	left hippocampus, right hippocampus, left am	33.7	8.9	29.8	10.1	7	12
Carrión VG	2001	http://dx.d	24	24	DSM-IV	ns	total brain, right brain, left brain, total cerebri	11	ns	11	ns	10	10
De_Bellis MD	2001	http://dx.d	9	9	DSM-IV	ns	cerebral volume, temporal lobe, total amygdal	10.6	1.6	10.5	1.6	4	4
Schuff N	2001	http://dx.d	18	19	DSM-IV	63.1	left hippocampus, right hippocampus, left ento	51.2	2.5	51.8	3.2	0	0
De_Bellis MD	2002	http://dx.d	28	66	DSM-IV	ns	intracranial volume, cerebral volume, cortical	11.47	3	11.58	2.83	14	35
De_Bellis MD	2002	http://dx.d	43	61	DSM-IV	ns	total superior temporal gyrus (STG), total righ	12.2	2.4	12	2.3	18	25
Fennema-Notest	2002	http://dx.d	11	17	DSM-IV	58	bilateral mesial temporal lobe (MTL) gray, left	33.35	10.3	35.3	12.5	11	17
Gilbertson MW	2002	http://www	12	23	DSM-IV	72.2	total brain volume, total hippocampus, right hi	ns	ns	ns	ns	0	0
Villareal G	2002	http://dx.d	12	10	DSM-IV	87	right hippocampus, left hippocampus, right hi	43	9.3	44	11.4	10	8
Bremner JD	2003	http://ajp.r	10	11	DSM-IV	ns	left hippocampus, right hippocampus, total br	35	6	32	8	10	11
De_Bellis MD	2003	http://dx.d	61	122	DSM-IV	ns	intracranial volume, cerebral volume, cerebra	11.74	2.63	11.71	2.56	30	60
Hedges DW	2003	http://jour	4	4	DSM-IV	ns	total brain volume, total hippocampal volume	54.5	6	54.3	7.09	0	0
Rauch SL	2003	http://www	9	9	DSM-IV	70.8	total cortical volume, pregenual anterior cingi	52	1.9	51.7	1.9	9	9
Yamasue H	2003	http://dx.d	9	16	CAPS	62.2	VBM gray, VBM white	44.6	16	44.4	14	4	6

Hippocampus			Summary		
SD for Effect size	1	input=	Pooled SD		
Measure (L,R,T)	total	input=	Total		
Hedges Correction	1	input=	H Correction		
Volume effect size	0	input=	Cohens Effect size		
Number of studies	41				
Number patients	909	Correlation	0.8		
Number of controls	991				
Heterogeneity (Q)	105.32	Publication Bias			
I ² %	62.0				
p value	0.000	p value	0.012		
Fixed Effects	-0.402				
(-95% to +95%)	-0.496		-0.308		
FFX p	0.000				
Random Effects	-0.473				
(-95% to +95%)	-0.635		-0.311		
RFX p	0.000				



Intracranial Volume			Summary		
SD for Effect size	1	input=	Pooled SD		
Measure (L,R,T)	Total	input=	Total		
Hedges Correction	1	input=	H Correction		
Volume effect size	0	input=	Cohens Effect size		
Number of studies	13				
Number patients	224	Correlation	0.8		
Number of controls	248				
Heterogeneity (Q)	16.70	Publication Bias			
I ² %	10.2				
p value	0.337	p value	0.112		
Fixed Effects	-0.238				
(-95% to +95%)	-0.415		-0.060		
FFX p	0.009				
Random Effects	-0.244				
(-95% to +95%)	-0.432		-0.055		
RFX p	0.012				

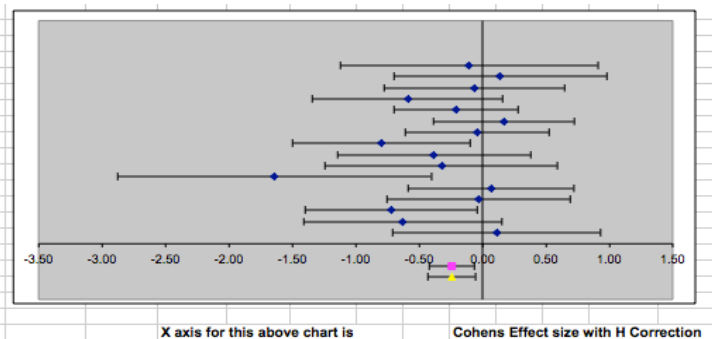


Figure S15: Screenshot of online database available at and meta-analysis available at www.ptsdmri.uk. The top part of the database is shown followed by a section of the meta-analysis page of the hippocampus and Intracranial volume showing forest plots and results.

References for Supplementary Materials and Papers Included in Database

References 1- 8 are citations from the supplementary materials while paper and subsequent references are papers included in the database.

1. Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, Charney DS, Keane TM. The development of a Clinician-Administered PTSD Scale. *J Trauma Stress*. 1995;8:75-90.
2. Koolschijn PC, van Haren NE, Lensvelt-Mulders GJ, Hulshoff Pol HE, Kahn RS. Brain volume abnormalities in major depressive disorder: a meta-analysis of magnetic resonance imaging studies. *Human brain mapping*. 2009;30:3719-3735.
3. Bradburn MJ, Deeks JJ, DG. A. Metan-an alternative meta-analysis command. *Stata Technical Bulletin*. 1999;8.
4. Kempton MJ, Salvador Z, Munafo MR, Geddes JR, Simmons A, Frangou S, Williams SC. Structural neuroimaging studies in major depressive disorder. Meta-analysis and comparison with bipolar disorder. *Archives of general psychiatry*. 2011;68:675-690.
5. Kempton MJ, Geddes JR, Ettinger U, Williams SC, Grasby PM. Meta-analysis, database, and meta-regression of 98 structural imaging studies in bipolar disorder. *Archives of general psychiatry*. 2008;65:1017-1032.
6. Kempton MJ, Stahl D, Williams SC, DeLisi LE. Progressive lateral ventricular enlargement in schizophrenia: a meta-analysis of longitudinal MRI studies. *Schizophrenia research*. 2010;120:54-62.
7. Wright IC, Rabe-Hesketh S, Woodruff PW, David AS, Murray RM, Bullmore ET. Meta-analysis of regional brain volumes in schizophrenia. *The American journal of psychiatry*. 2000;157:16-25.
8. Radua J, Mataix-Cols D, Phillips ML, El-Hage W, Kronhaus DM, Cardoner N, Surguladze S. A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps. *European psychiatry : the journal of the Association of European Psychiatrists*. 2012;27:605-611.
9. Bremner JD, Randall P, Scott TM, Bronen RA, Seibyl JP, Southwick SM, Delaney RC, McCarthy G, Charney DS, Innis RB. MRI-based measurement of hippocampal volume in patients with combat-related posttraumatic stress disorder. *The American journal of psychiatry*. 1995;152:973-981.
10. Gurvits TV, Shenton ME, Hokama H, Ohta H, Lasko NB, Gilbertson MW, Orr SP, Kikinis R, Jolesz FA, McCarley RW, Pitman RK. Magnetic resonance imaging study of hippocampal volume in chronic, combat-related posttraumatic stress disorder. *Biological psychiatry*. 1996;40:1091-1099.
11. Bremner JD, Randall P, Vermetten E, Staib L, Bronen RA, Mazure C, Capelli S, McCarthy G, Innis RB, Charney DS. Magnetic resonance imaging-based measurement of hippocampal volume in posttraumatic stress disorder related to childhood physical and sexual abuse--a preliminary report. *Biological psychiatry*. 1997;41:23-32.
12. De Bellis MD, Keshavan MS, Clark DB, Casey BJ, Giedd JN, Boring AM, Frustaci K, Ryan ND. A.E. Bennett Research Award. Developmental traumatology. Part II: Brain development. *Biological psychiatry*. 1999;45:1271-1284.
13. Bonne O, Brandes D, Gilboa A, Gomori JM, Shenton ME, Pitman RK, Shalev AY. Longitudinal MRI study of hippocampal volume in trauma survivors with PTSD. *The American journal of psychiatry*. 2001;158:1248-1251.
14. Carrion VG, Weems CF, Eliez S, Patwardhan A, Brown W, Ray RD, Reiss AL. Attenuation of frontal asymmetry in pediatric posttraumatic stress disorder. *Biological psychiatry*. 2001;50:943-951.

15. De Bellis MD, Hall J, Boring AM, Frustaci K, Moritz G. A pilot longitudinal study of hippocampal volumes in pediatric maltreatment-related posttraumatic stress disorder. *Biological psychiatry*. 2001;50:305-309.
16. Schuff N, Neylan TC, Lenoci MA, Du AT, Weiss DS, Marmar CR, Weiner MW. Decreased hippocampal N-acetylaspartate in the absence of atrophy in posttraumatic stress disorder. *Biological psychiatry*. 2001;50:952-959.
17. De Bellis MD, Keshavan MS, Frustaci K, Shifflett H, Iyengar S, Beers SR, Hall J. Superior temporal gyrus volumes in maltreated children and adolescents with PTSD. *Biological psychiatry*. 2002;51:544-552.
18. De Bellis MD, Keshavan MS, Shifflett H, Iyengar S, Beers SR, Hall J, Moritz G. Brain structures in pediatric maltreatment-related posttraumatic stress disorder: a sociodemographically matched study. *Biological psychiatry*. 2002;52:1066-1078.
19. Fennema-Notestine C, Stein MB, Kennedy CM, Archibald SL, Jernigan TL. Brain morphometry in female victims of intimate partner violence with and without posttraumatic stress disorder. *Biological psychiatry*. 2002;52:1089-1101.
20. Gilbertson MW, Shenton ME, Ciszewski A, Kasai K, Lasko NB, Orr SP, Pitman RK. Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. *Nature neuroscience*. 2002;5:1242-1247.
21. Villarreal G, Hamilton DA, Petropoulos H, Driscoll I, Rowland LM, Griego JA, Kodituwakku PW, Hart BL, Escalona R, Brooks WM. Reduced hippocampal volume and total white matter volume in posttraumatic stress disorder. *Biological psychiatry*. 2002;52:119-125.
22. Bremner JD, Vythilingam M, Vermetten E, Southwick SM, McGlashan T, Nazeer A, Khan S, Vaccarino LV, Soufer R, Garg PK, Ng CK, Staib LH, Duncan JS, Charney DS. MRI and PET study of deficits in hippocampal structure and function in women with childhood sexual abuse and posttraumatic stress disorder. *The American journal of psychiatry*. 2003;160:924-932.
23. De Bellis MD, Keshavan MS. Sex differences in brain maturation in maltreatment-related pediatric posttraumatic stress disorder. *Neuroscience and biobehavioral reviews*. 2003;27:103-117.
24. Hedges DW, Allen S, Tate DF, Thatcher GW, Miller MJ, Rice SA, Cleavinger HB, Sood S, Bigler ED. Reduced hippocampal volume in alcohol and substance naive Vietnam combat veterans with posttraumatic stress disorder. *Cognitive and behavioral neurology : official journal of the Society for Behavioral and Cognitive Neurology*. 2003;16:219-224.
25. Rauch SL, Shin LM, Segal E, Pitman RK, Carson MA, McMullin K, Whalen PJ, Makris N. Selectively reduced regional cortical volumes in post-traumatic stress disorder. *Neuroreport*. 2003;14:913-916.
26. Yamasue H, Kasai K, Iwanami A, Ohtani T, Yamada H, Abe O, Kuroki N, Fukuda R, Tochigi M, Furukawa S, Sadamatsu M, Sasaki T, Aoki S, Ohtomo K, Asukai N, Kato N. Voxel-based analysis of MRI reveals anterior cingulate gray-matter volume reduction in posttraumatic stress disorder due to terrorism. *Proceedings of the National Academy of Sciences of the United States of America*. 2003;100:9039-9043.
27. Lindauer RJ, Vlieger EJ, Jalink M, Olff M, Carlier IV, Majoie CB, den Heeten GJ, Gersons BP. Smaller hippocampal volume in Dutch police officers with posttraumatic stress disorder. *Biological psychiatry*. 2004;56:356-363.
28. May FS, Chen QC, Gilbertson MW, Shenton ME, Pitman RK. Cavum septum pellucidum in monozygotic twins discordant for combat exposure: relationship to posttraumatic stress disorder. *Biological psychiatry*. 2004;55:656-658.

29. Pederson CL, Maurer SH, Kaminski PL, Zander KA, Peters CM, Stokes-Crowe LA, Osborn RE. Hippocampal volume and memory performance in a community-based sample of women with posttraumatic stress disorder secondary to child abuse. *J Trauma Stress*. 2004;17:37-40.
30. Shin LM, Shin PS, Heckers S, Krangel TS, Macklin ML, Orr SP, Lasko N, Segal E, Makris N, Richert K, Levering J, Schacter DL, Alpert NM, Fischman AJ, Pitman RK, Rauch SL. Hippocampal function in posttraumatic stress disorder. *Hippocampus*. 2004;14:292-300.
31. Thomas LA, De Bellis MD. Pituitary volumes in pediatric maltreatment-related posttraumatic stress disorder. *Biological psychiatry*. 2004;55:752-758.
32. Villarreal G, Hamilton DA, Graham DP, Driscoll I, Qualls C, Petropoulos H, Brooks WM. Reduced area of the corpus callosum in posttraumatic stress disorder. *Psychiatry research*. 2004;131:227-235.
33. Wignall EL, Dickson JM, Vaughan P, Farrow TF, Wilkinson ID, Hunter MD, Woodruff PW. Smaller hippocampal volume in patients with recent-onset posttraumatic stress disorder. *Biological psychiatry*. 2004;56:832-836.
34. Winter H, Irle E. Hippocampal volume in adult burn patients with and without posttraumatic stress disorder. *The American journal of psychiatry*. 2004;161:2194-2200.
35. Corbo V, Clement MH, Armony JL, Pruessner JC, Brunet A. Size versus shape differences: contrasting voxel-based and volumetric analyses of the anterior cingulate cortex in individuals with acute posttraumatic stress disorder. *Biological psychiatry*. 2005;58:119-124.
36. Golier JA, Yehuda R, De Santi S, Segal S, Dolan S, de Leon MJ. Absence of hippocampal volume differences in survivors of the Nazi Holocaust with and without posttraumatic stress disorder. *Psychiatry research*. 2005;139:53-64.
37. Lindauer RJ, Vlieger EJ, Jalink M, Olff M, Carlier IV, Majoie CB, Den Heeten GJ, Gersons BP. Effects of psychotherapy on hippocampal volume in out-patients with post-traumatic stress disorder: a MRI investigation. *Psychological medicine*. 2005;35:1421-1431.
38. Vythilingam M, Luckenbaugh DA, Lam T, Morgan CA, 3rd, Lipschitz D, Charney DS, Bremner JD, Southwick SM. Smaller head of the hippocampus in Gulf War-related posttraumatic stress disorder. *Psychiatry research*. 2005;139:89-99.
39. Chen S, Xia W, Li L, Liu J, He Z, Zhang Z, Yan L, Zhang J, Hu D. Gray matter density reduction in the insula in fire survivors with posttraumatic stress disorder: a voxel-based morphometric study. *Psychiatry research*. 2006;146:65-72.
40. De Bellis MD, Kuchibhatla M. Cerebellar volumes in pediatric maltreatment-related posttraumatic stress disorder. *Biological psychiatry*. 2006;60:697-703.
41. Emdad R, Bonekamp D, Sondergaard HP, Bjorklund T, Agartz I, Ingvar M, Theorell T. Morphometric and psychometric comparisons between non-substance-abusing patients with posttraumatic stress disorder and normal controls. *Psychother Psychosom*. 2006;75:122-132.
42. Freeman T, Kimbrell T, Booe L, Myers M, Cardwell D, Lindquist DM, Hart J, Komoroski RA. Evidence of resilience: neuroimaging in former prisoners of war. *Psychiatry research*. 2006;146:59-64.
43. Jatzko A, Rothenhofer S, Schmitt A, Gaser C, Demirakca T, Weber-Fahr W, Wessa M, Magnotta V, Braus DF. Hippocampal volume in chronic posttraumatic stress disorder (PTSD): MRI study using two different evaluation methods. *Journal of affective disorders*. 2006;94:121-126.
44. Kitayama N, Quinn S, Bremner JD. Smaller volume of anterior cingulate cortex in abuse-related posttraumatic stress disorder. *Journal of affective disorders*. 2006;90:171-174.
45. Levitt JJ, Chen QC, May FS, Gilbertson MW, Shenton ME, Pitman RK. Volume of cerebellar vermis in monozygotic twins discordant for combat exposure: lack of relationship to post-traumatic stress disorder. *Psychiatry research*. 2006;148:143-149.

46. Li L, Chen S, Liu J, Zhang J, He Z, Lin X. Magnetic resonance imaging and magnetic resonance spectroscopy study of deficits in hippocampal structure in fire victims with recent-onset posttraumatic stress disorder. *Can J Psychiatry*. 2006;51:431-437.
47. Lindauer RJ, Olff M, van Meijel EP, Carlier IV, Gersons BP. Cortisol, learning, memory, and attention in relation to smaller hippocampal volume in police officers with posttraumatic stress disorder. *Biological psychiatry*. 2006;59:171-177.
48. Richert KA, Carrion VG, Karchemskiy A, Reiss AL. Regional differences of the prefrontal cortex in pediatric PTSD: an MRI study. *Depress Anxiety*. 2006;23:17-25.
49. Tupler LA, De Bellis MD. Segmented hippocampal volume in children and adolescents with posttraumatic stress disorder. *Biological psychiatry*. 2006;59:523-529.
50. Woodward SH, Kaloupek DG, Streeter CC, Martinez C, Schaer M, Eliez S. Decreased anterior cingulate volume in combat-related PTSD. *Biological psychiatry*. 2006;59:582-587.
51. Hakamata Y, Matsuoka Y, Inagaki M, Nagamine M, Hara E, Imoto S, Murakami K, Kim Y, Uchitomi Y. Structure of orbitofrontal cortex and its longitudinal course in cancer-related post-traumatic stress disorder. *Neurosci Res*. 2007;59:383-389.
52. Kitayama N, Brummer M, Hertz L, Quinn S, Kim Y, Bremner JD. Morphologic alterations in the corpus callosum in abuse-related posttraumatic stress disorder: a preliminary study. *J Nerv Ment Dis*. 2007;195:1027-1029.
53. Pavic L, Gregurek R, Rados M, Brkljacic B, Brajkovic L, Simetin-Pavic I, Ivanac G, Pavlisa G, Kalousek V. Smaller right hippocampus in war veterans with posttraumatic stress disorder. *Psychiatry research*. 2007;154:191-198.
54. Woodward SH, Kaloupek DG, Streeter CC, Kimble MO, Reiss AL, Eliez S, Wald LL, Renshaw PF, Frederick BB, Lane B, Sheikh JI, Stegman WK, Kutter CJ, Stewart LP, Prestel RS, Arsenault NJ. Brain, skull, and cerebrospinal fluid volumes in adult posttraumatic stress disorder. *J Trauma Stress*. 2007;20:763-774.
55. Yehuda R, Golier JA, Tischler L, Harvey PD, Newmark R, Yang RK, Buchsbaum MS. Hippocampal volume in aging combat veterans with and without post-traumatic stress disorder: relation to risk and resilience factors. *Journal of psychiatric research*. 2007;41:435-445.
56. Bonne O, Vythilingam M, Inagaki M, Wood S, Neumeister A, Nugent AC, Snow J, Luckenbaugh DA, Bain EE, Drevets WC, Charney DS. Reduced posterior hippocampal volume in posttraumatic stress disorder. *The Journal of clinical psychiatry*. 2008;69:1087-1091.
57. Bossini L, Tavanti M, Calossi S, Lombardelli A, Polizzotto NR, Galli R, Vatti G, Pieraccini F, Castrogiovanni P. Magnetic resonance imaging volumes of the hippocampus in drug-naive patients with post-traumatic stress disorder without comorbidity conditions. *Journal of psychiatric research*. 2008;42:752-762.
58. Bryant RA, Felmingham K, Whitford TJ, Kemp A, Hughes G, Peduto A, Williams LM. Rostral anterior cingulate volume predicts treatment response to cognitive-behavioural therapy for posttraumatic stress disorder. *Journal of psychiatry & neuroscience : JPN*. 2008;33:142-146.
59. Geuze E, Westenberg HG, Heinecke A, de Kloet CS, Goebel R, Vermetten E. Thinner prefrontal cortex in veterans with posttraumatic stress disorder. *NeuroImage*. 2008;41:675-681.
60. Hara E, Matsuoka Y, Hakamata Y, Nagamine M, Inagaki M, Imoto S, Murakami K, Kim Y, Uchitomi Y. Hippocampal and amygdalar volumes in breast cancer survivors with posttraumatic stress disorder. *The Journal of neuropsychiatry and clinical neurosciences*. 2008;20:302-308.
61. Kasai K, Yamasue H, Gilbertson MW, Shenton ME, Rauch SL, Pitman RK. Evidence for acquired pregenual anterior cingulate gray matter loss from a twin study of combat-related posttraumatic stress disorder. *Biological psychiatry*. 2008;63:550-556.

62. Schuff N, Neylan TC, Fox-Bosetti S, Lenoci M, Samuelson KW, Studholme C, Kornak J, Marmar CR, Weiner MW. Abnormal N-acetylaspartate in hippocampus and anterior cingulate in posttraumatic stress disorder. *Psychiatry research*. 2008;162:147-157.
63. Weniger G, Lange C, Sachsse U, Irle E. Amygdala and hippocampal volumes and cognition in adult survivors of childhood abuse with dissociative disorders. *Acta psychiatrica Scandinavica*. 2008;118:281-290.
64. Carrion VG, Weems CF, Watson C, Eliez S, Menon V, Reiss AL. Converging evidence for abnormalities of the prefrontal cortex and evaluation of midsagittal structures in pediatric posttraumatic stress disorder: an MRI study. *Psychiatry research*. 2009;172:226-234.
65. Chen S, Li L, Xu B, Liu J. Insular cortex involvement in declarative memory deficits in patients with post-traumatic stress disorder. *BMC psychiatry*. 2009;9:39.
66. Felmingham K, Williams LM, Whitford TJ, Falconer E, Kemp AH, Peduto A, Bryant RA. Duration of posttraumatic stress disorder predicts hippocampal grey matter loss. *Neuroreport*. 2009;20:1402-1406.
67. Looi JC, Maller JJ, Pagani M, Hogberg G, Lindberg O, Liberg B, Botes L, Engman EL, Zhang Y, Svensson L, Wahlund LO. Caudate volumes in public transportation workers exposed to trauma in the Stockholm train system. *Psychiatry research*. 2009;171:138-143.
68. Rogers MA, Yamasue H, Abe O, Yamada H, Ohtani T, Iwanami A, Aoki S, Kato N, Kasai K. Smaller amygdala volume and reduced anterior cingulate gray matter density associated with history of post-traumatic stress disorder. *Psychiatry research*. 2009;174:210-216.
69. Woodward SH, Schaer M, Kaloupek DG, Cediell L, Eliez S. Smaller global and regional cortical volume in combat-related posttraumatic stress disorder. *Archives of general psychiatry*. 2009;66:1373-1382.
70. Carrion VG, Weems CF, Richert K, Hoffman BC, Reiss AL. Decreased prefrontal cortical volume associated with increased bedtime cortisol in traumatized youth. *Biological psychiatry*. 2010;68:491-493.
71. Landre L, Destrieux C, Baudry M, Barantin L, Cottier JP, Martineau J, Hommet C, Isingrini M, Belzung C, Gaillard P, Camus V, El Hage W. Preserved subcortical volumes and cortical thickness in women with sexual abuse-related PTSD. *Psychiatry research*. 2010;183:181-186.
72. Nardo D, Hogberg G, Looi JC, Larsson S, Hallstrom T, Pagani M. Gray matter density in limbic and paralimbic cortices is associated with trauma load and EMDR outcome in PTSD patients. *Journal of psychiatric research*. 2010;44:477-485.
73. Sui SG, Wu MX, King ME, Zhang Y, Ling L, Xu JM, Weng XC, Duan L, Shan BC, Li LJ. Abnormal grey matter in victims of rape with PTSD in Mainland China: a voxel-based morphometry study. *Acta Neuropsychiatr*. 2010;22:118-126.
74. Sui SG, Zhang Y, Wu MX, Xu JM, Duan L, Weng XC, Shan BC, Li LJ. Abnormal cerebellum density in victims of rape with post-traumatic stress disorder: Voxel-based analysis of magnetic resonance imaging investigation. *Asia-Pac Psychiat*. 2010;2:129-135.
75. Thomaes K, Dorrepaal E, Draijer N, de Ruiter MB, van Balkom AJ, Smit JH, Veltman DJ. Reduced anterior cingulate and orbitofrontal volumes in child abuse-related complex PTSD. *The Journal of clinical psychiatry*. 2010;71:1636-1644.
76. Wang Z, Neylan TC, Mueller SG, Lenoci M, Truran D, Marmar CR, Weiner MW, Schuff N. Magnetic resonance imaging of hippocampal subfields in posttraumatic stress disorder. *Archives of general psychiatry*. 2010;67:296-303.
77. Apfel BA, Ross J, Hlavin J, Meyerhoff DJ, Metzler TJ, Marmar CR, Weiner MW, Schuff N, Neylan TC. Hippocampal volume differences in Gulf War veterans with current versus lifetime posttraumatic stress disorder symptoms. *Biological psychiatry*. 2011;69:541-548.

78. Baldacara L, Jackowski AP, Schoedl A, Pupo M, Andreoli SB, Mello MF, Lacerda AL, Mari JJ, Bressan RA. Reduced cerebellar left hemisphere and vermal volume in adults with PTSD from a community sample. *Journal of psychiatric research*. 2011;45:1627-1633.
79. Eckart C, Stoppel C, Kaufmann J, Tempelmann C, Hinrichs H, Elbert T, Heinze HJ, Kolassa IT. Structural alterations in lateral prefrontal, parietal and posterior midline regions of men with chronic posttraumatic stress disorder. *Journal of psychiatry & neuroscience : JPN*. 2011;36:176-186.
80. Hunter M, Villarreal G, McHaffie GR, Jimenez B, Smith AK, Calais LA, Hanlon F, Thoma RJ, Canive JM. Lateralized abnormalities in auditory M50 sensory gating and cortical thickness of the superior temporal gyrus in post-traumatic stress disorder: preliminary results. *Psychiatry research*. 2011;191:138-144.
81. Lyoo IK, Kim JE, Yoon SJ, Hwang J, Bae S, Kim DJ. The neurobiological role of the dorsolateral prefrontal cortex in recovery from trauma. Longitudinal brain imaging study among survivors of the South Korean subway disaster. *Archives of general psychiatry*. 2011;68:701-713.
82. Savitz JB, Bonne O, Nugent AC, Vythilingam M, Bogers W, Charney DS, Drevets WC. Habenula volume in post-traumatic stress disorder measured with high-resolution MRI. *Biol Mood Anxiety Disord*. 2011;1:7.
83. Schulz-Heik RJ, Schaer M, Eliez S, Hallmayer JF, Lin X, Kaloupek DG, Woodward SH. Catechol-O-methyltransferase Val158Met polymorphism moderates anterior cingulate volume in posttraumatic stress disorder. *Biological psychiatry*. 2011;70:1091-1096.
84. Zhang J, Tan Q, Yin H, Zhang X, Huan Y, Tang L, Wang H, Xu J, Li L. Decreased gray matter volume in the left hippocampus and bilateral calcarine cortex in coal mine flood disaster survivors with recent onset PTSD. *Psychiatry research*. 2011;192:84-90.
85. Ahmed F, Spottiswoode BS, Carey PD, Stein DJ, Seedat S. Relationship between neurocognition and regional brain volumes in traumatized adolescents with and without posttraumatic stress disorder. *Neuropsychobiology*. 2012;66:174-184.
86. Chao LL, Lenoci M, Neylan TC. Effects of post-traumatic stress disorder on occipital lobe function and structure. *Neuroreport*. 2012;23:412-419.
87. Chen Y, Fu K, Feng C, Tang L, Zhang J, Huan Y, Cui J, Mu Y, Qi S, Xiong L, Ma C, Wang H, Tan Q, Yin H. Different regional gray matter loss in recent onset PTSD and non PTSD after a single prolonged trauma exposure. *PloS one*. 2012;7:e48298.
88. Eckart C, Kaufmann J, Kanowski M, Tempelmann C, Hinrichs H, Elbert T, Heinze HJ, Kolassa IT. Magnetic resonance volumetry and spectroscopy of hippocampus and insula in relation to severe exposure of traumatic stress. *Psychophysiology*. 2012;49:261-270.
89. Herringa R, Phillips M, Almeida J, Insana S, Germain A. Post-traumatic stress symptoms correlate with smaller subgenual cingulate, caudate, and insula volumes in unmedicated combat veterans. *Psychiatry research*. 2012;203:139-145.
90. Kuo JR, Kaloupek DG, Woodward SH. Amygdala volume in combat-exposed veterans with and without posttraumatic stress disorder: a cross-sectional study. *Archives of general psychiatry*. 2012;69:1080-1086.
91. Morey RA, Gold AL, LaBar KS, Beall SK, Brown VM, Haswell CC, Nasser JD, Wagner HR, McCarthy G, Mid-Atlantic MW. Amygdala volume changes in posttraumatic stress disorder in a large case-controlled veterans group. *Archives of general psychiatry*. 2012;69:1169-1178.
92. Rocha-Rego V, Pereira MG, Oliveira L, Mendlowicz MV, Fisman A, Marques-Portella C, Berger W, Chu C, Joffily M, Moll J, Mari JJ, Figueira I, Volchan E. Decreased premotor cortex volume in victims of urban violence with posttraumatic stress disorder. *PloS one*. 2012;7:e42560.
93. Tavanti M, Battaglini M, Borgogni F, Bossini L, Calossi S, Marino D, Vatti G, Pieraccini F, Federico A, Castrogiovanni P, De Stefano N. Evidence of diffuse damage in frontal and occipital cortex in

- the brain of patients with post-traumatic stress disorder. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*. 2012;33:59-68.
94. Chao L, Weiner M, Neylan T. Regional cerebral volumes in veterans with current versus remitted posttraumatic stress disorder. *Psychiatry research*. 2013;213:193-201.
 95. Jatzko A, Vogler C, Demirakca T, Ruf M, Malchow B, Falkai P, Braus DF, Ende G, Schmitt A. Pattern and volume of the anterior cingulate cortex in chronic posttraumatic stress disorder (PTSD). *Eur Arch Psychiatry Clin Neurosci*. 2013;263:585-592.
 96. Nardo D, Hogberg G, Lanius RA, Jacobsson H, Jonsson C, Hallstrom T, Pagani M. Gray matter volume alterations related to trait dissociation in PTSD and traumatized controls. *Acta psychiatrica Scandinavica*. 2013;128:222-233.
 97. Shu XJ, Xue L, Liu W, Chen FY, Zhu C, Sun XH, Wang XP, Liu ZC, Zhao H. More vulnerability of left than right hippocampal damage in right-handed patients with post-traumatic stress disorder. *Psychiatry research*. 2013;212:237-244.
 98. Tan L, Zhang L, Qi R, Lu G, Li L, Liu J, Li W. Brain structure in post-traumatic stress disorder: A voxel-based morphometry analysis. *Neural Regen Res*. 2013;8:2405-2414.
 99. Weems CF, Scott BG, Russell JD, Reiss AL, Carrion VG. Developmental variation in amygdala volumes among children with posttraumatic stress. *Dev Neuropsychol*. 2013;38:481-495.
 100. Baldacara L, Zugman A, Araujo C, Cogo-Moreira H, Lacerda AL, Schoedl A, Pupo M, Mello MF, Andreoli SB, de Jesus Mari J, Bressan RA, Jackowski AP. Reduction of anterior cingulate in adults with urban violence-related PTSD. *Journal of affective disorders*. 2014;168:13-20.
 101. Starcevic A, Postic S, Radojicic Z, Starcevic B, Milovanovic S, Ilankovic A, Dimitrijevic I, Damjanovic A, Aksic M, Radonjic V. Volumetric analysis of amygdala, hippocampus, and prefrontal cortex in therapy-naïve PTSD participants. *Biomed Res Int*. 2014;2014:968495.
 102. Zhang Q, Zhuo C, Lang X, Li H, Qin W, Yu C. Structural impairments of hippocampus in coal mine gas explosion-related posttraumatic stress disorder. *PloS one*. 2014;9:e102042.
 103. Chalavi S, Vissia EM, Giesen ME, Nijenhuis ER, Draijer N, Barker GJ, Veltman DJ, Reinders AA. Similar cortical but not subcortical gray matter abnormalities in women with posttraumatic stress disorder with versus without dissociative identity disorder. *Psychiatry research*. 2015;231:308-319.
 104. Chalavi S, Vissia EM, Giesen ME, Nijenhuis ER, Draijer N, Cole JH, Dazzan P, Pariante CM, Madsen SK, Rajagopalan P, Thompson PM, Toga AW, Veltman DJ, Reinders AA. Abnormal hippocampal morphology in dissociative identity disorder and post-traumatic stress disorder correlates with childhood trauma and dissociative symptoms. *Human brain mapping*. 2015;36:1692-1704.
 105. Cheng B, Huang X, Li S, Hu X, Luo Y, Wang X, Yang X, Qiu C, Yang Y, Zhang W, Bi F, Roberts N, Gong Q. Gray Matter Alterations in Post-Traumatic Stress Disorder, Obsessive-Compulsive Disorder, and Social Anxiety Disorder. *Front Behav Neurosci*. 2015;9:219.
 106. Cortese BM, McConnell PA, Froeliger B, Leslie K, Uhde TW. Burning odor-elicited anxiety in OEF/OIF combat veterans: Inverse relationship to gray matter volume in olfactory cortex. *Journal of psychiatric research*. 2015;70:58-66.
 107. De Bellis MD, Hooper SR, Chen SD, Provenza JM, Boyd BD, Glessner CE, MacFall JR, Payne ME, Rybczynski R, Woolley DP. Posterior structural brain volumes differ in maltreated youth with and without chronic posttraumatic stress disorder. *Dev Psychopathol*. 2015;27:1555-1576.
 108. Demers LA, Olson EA, Crowley DJ, Rauch SL, Rosso IM. Dorsal Anterior Cingulate Thickness Is Related to Alexithymia in Childhood Trauma-Related PTSD. *PloS one*. 2015;10:e0139807.
 109. Keding TJ, Herringa RJ. Abnormal structure of fear circuitry in pediatric post-traumatic stress disorder. *Neuropsychopharmacology*. 2015;40:537-545.

110. Levy-Gigi E, Szabo C, Richter-Levin G, Keri S. Reduced hippocampal volume is associated with overgeneralization of negative context in individuals with PTSD. *Neuropsychology*. 2015;29:151-161.
111. Mueller SG, Ng P, Neylan T, Mackin S, Wolkowitz O, Mellon S, Yan X, Flory J, Yehuda R, Marmar CR, Weiner MW. Evidence for disrupted gray matter structural connectivity in posttraumatic stress disorder. *Psychiatry research*. 2015;234:194-201.
112. Nardo D, Hogberg G, Jonsson C, Jacobsson H, Hallstrom T, Pagani M. Neurobiology of Sleep Disturbances in PTSD Patients and Traumatized Controls: MRI and SPECT Findings. *Front Psychiatry*. 2015;6:134.
113. Starcevic A, Dimitrijevic I, Aksic M, Stijak L, Radonjic V, Aleksic D, Filipovic B. Brain changes in patients with posttraumatic stress disorder and associated alcoholism: MRI based study. *Psychiatr Danub*. 2015;27:78-83.
114. Veer IM, Oei NY, van Buchem MA, Spinhoven P, Elzinga BM, Rombouts SA. Evidence for smaller right amygdala volumes in posttraumatic stress disorder following childhood trauma. *Psychiatry research*. 2015;233:436-442.
115. Helpman L, Papini S, Chhetry BT, Shvil E, Rubin M, Sullivan GM, Markowitz JC, Mann JJ, Neria Y. Ptsd Remission after Prolonged Exposure Treatment Is Associated with Anterior Cingulate Cortex Thinning and Volume Reduction. *Depress Anxiety*. 2016;33:384-391.
116. Li S, Huang X, Li L, Du F, Li J, Bi F, Lui S, Turner JA, Sweeney JA, Gong Q. Posttraumatic Stress Disorder: Structural Characterization with 3-T MR Imaging. *Radiology*. 2016;280:537-544.
117. Luo Y, Shan H, Liu Y, Wu L, Zhang X, Ma T, Zhu W, Yang Y, Wang J, Cao Z. Decreased left hippocampal volumes in parents with or without posttraumatic stress disorder who lost their only child in China. *Journal of affective disorders*. 2016;197:223-230.
118. Morey RA, Haswell CC, Hooper SR, De Bellis MD. Amygdala, Hippocampus, and Ventral Medial Prefrontal Cortex Volumes Differ in Maltreated Youth with and without Chronic Posttraumatic Stress Disorder. *Neuropsychopharmacology*. 2016;41:791-801.
119. Rubin M, Shvil E, Papini S, Chhetry BT, Helpman L, Markowitz JC, Mann JJ, Neria Y. Greater hippocampal volume is associated with PTSD treatment response. *Psychiatry Res Neuroimaging*. 2016;252:36-39.
120. Sussman D, Pang EW, Jetly R, Dunkley BT, Taylor MJ. Neuroanatomical features in soldiers with post-traumatic stress disorder. *BMC Neurosci*. 2016;17:13.
121. Zandieh S, Bernt R, Knoll P, Wenzel T, Hittmair K, Haller J, Hergan K, Mirzaei S. Analysis of the Metabolic and Structural Brain Changes in Patients With Torture-Related Post-Traumatic Stress Disorder (TR-PTSD) Using (1)(8)F-FDG PET and MRI. *Medicine (Baltimore)*. 2016;95:e3387.